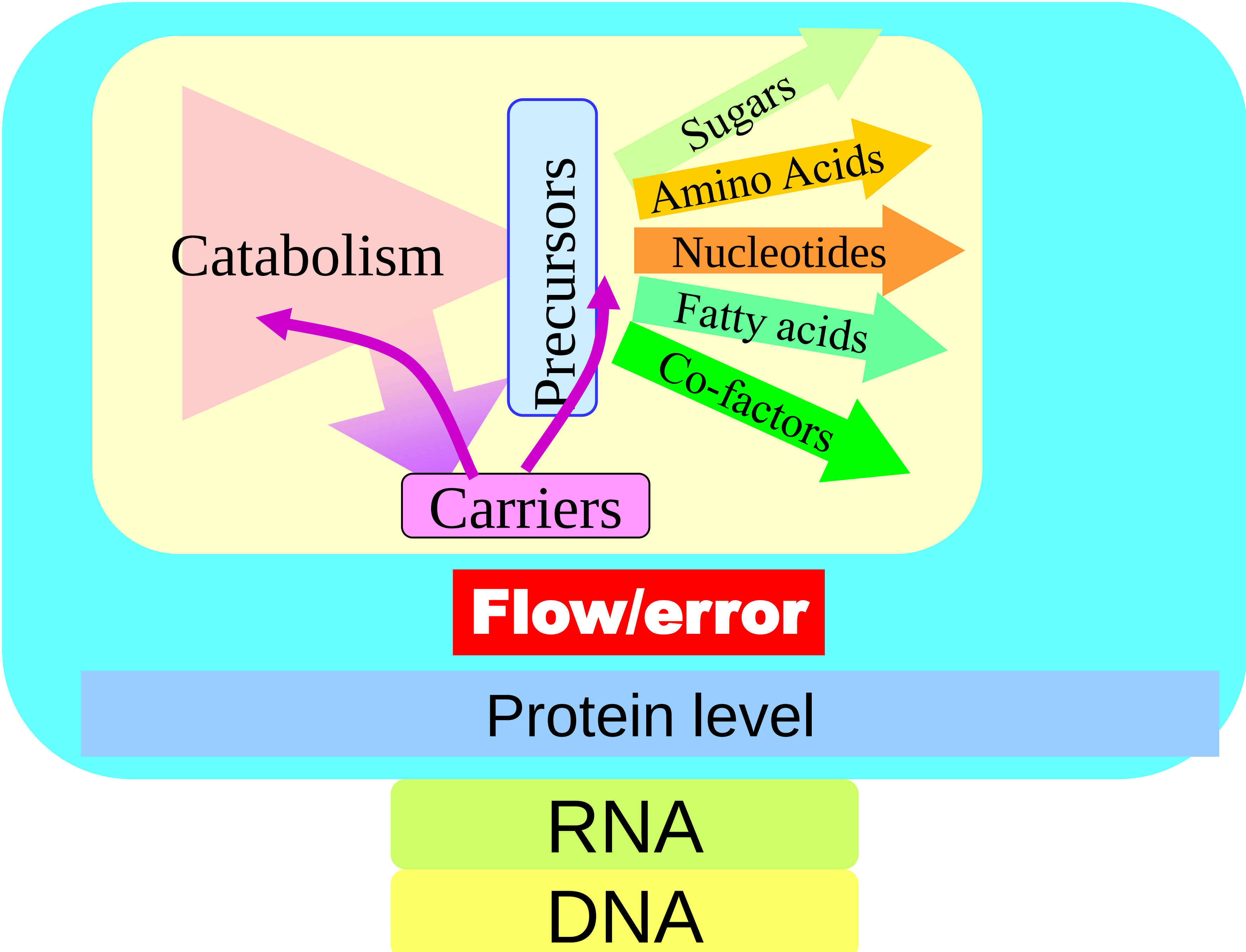
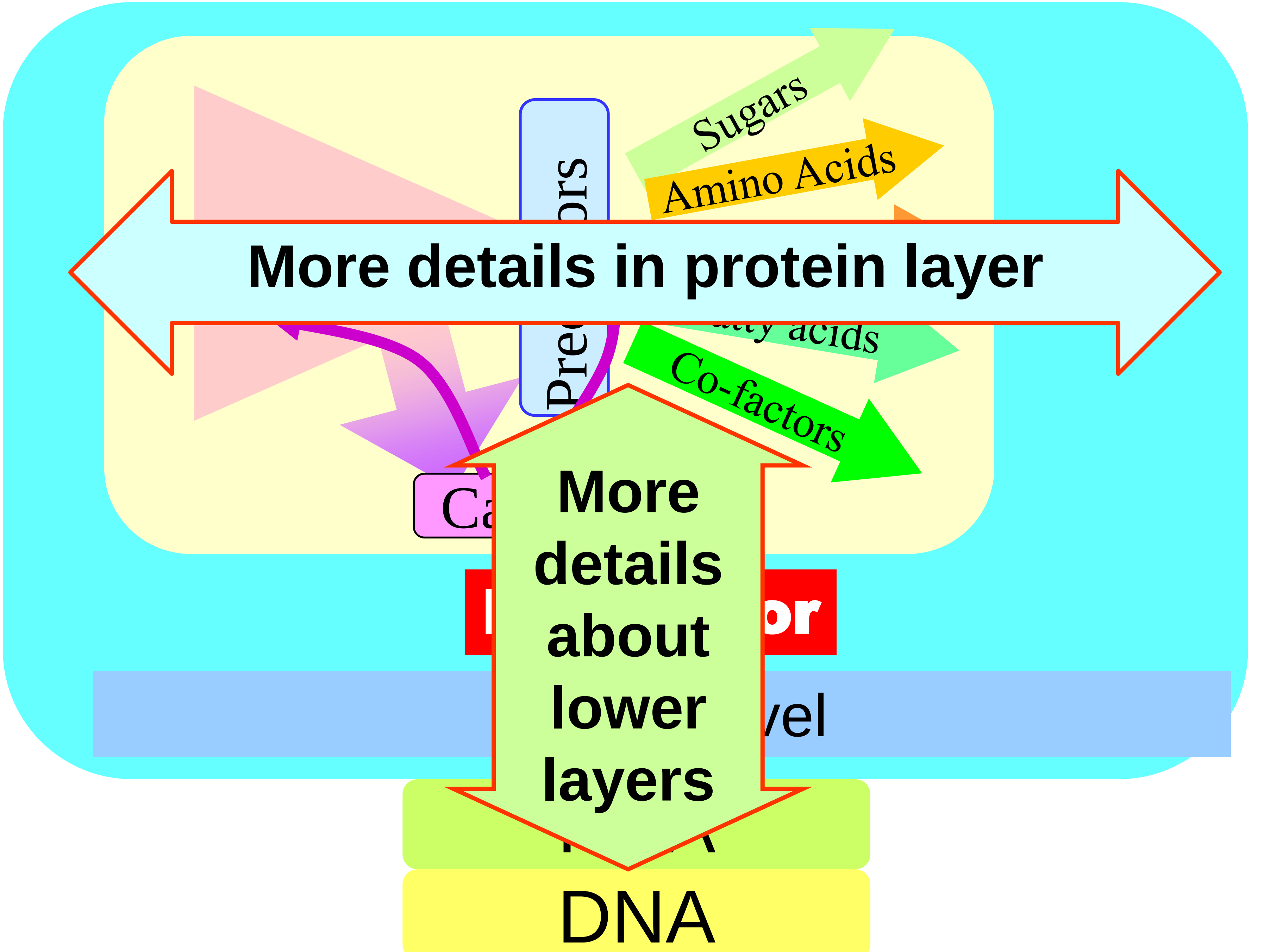


Catabolism
Precursors
Sugars
Amino Acids
Nucleotides
Fatty acids
Co-factors
Carriers
Flow/error
Protein level
RNA
DNA



More details in protein layer
More details about lower layers
Sugars
Amino Acids
Co-factors
DNA

In the much simpler world of the Internet, the details are still bewilderingly complex.

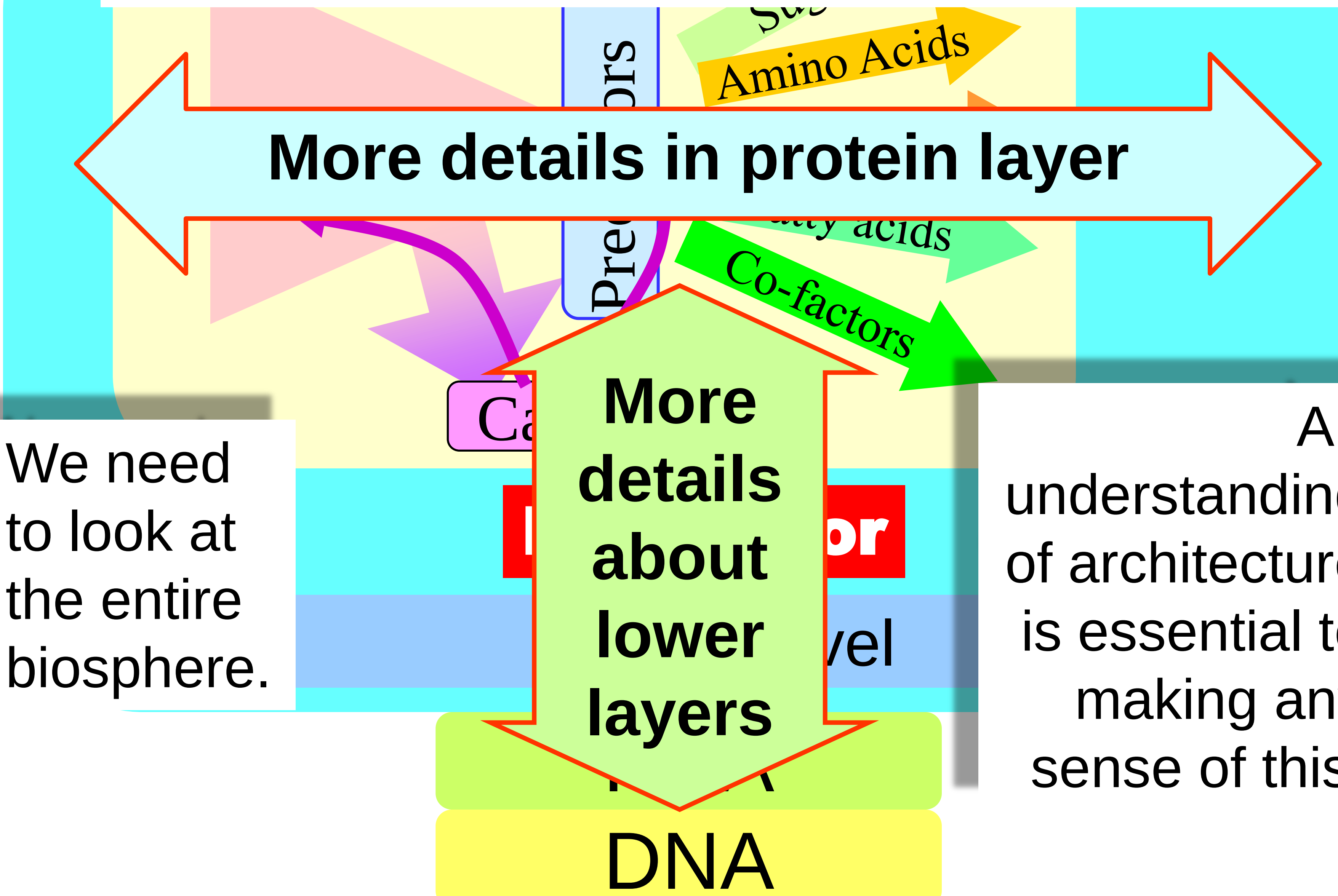
More details in application software

More details about the hardware design and supply chain

We'd need to look at the entire industry.

An understanding of architecture is essential to making any sense of this.

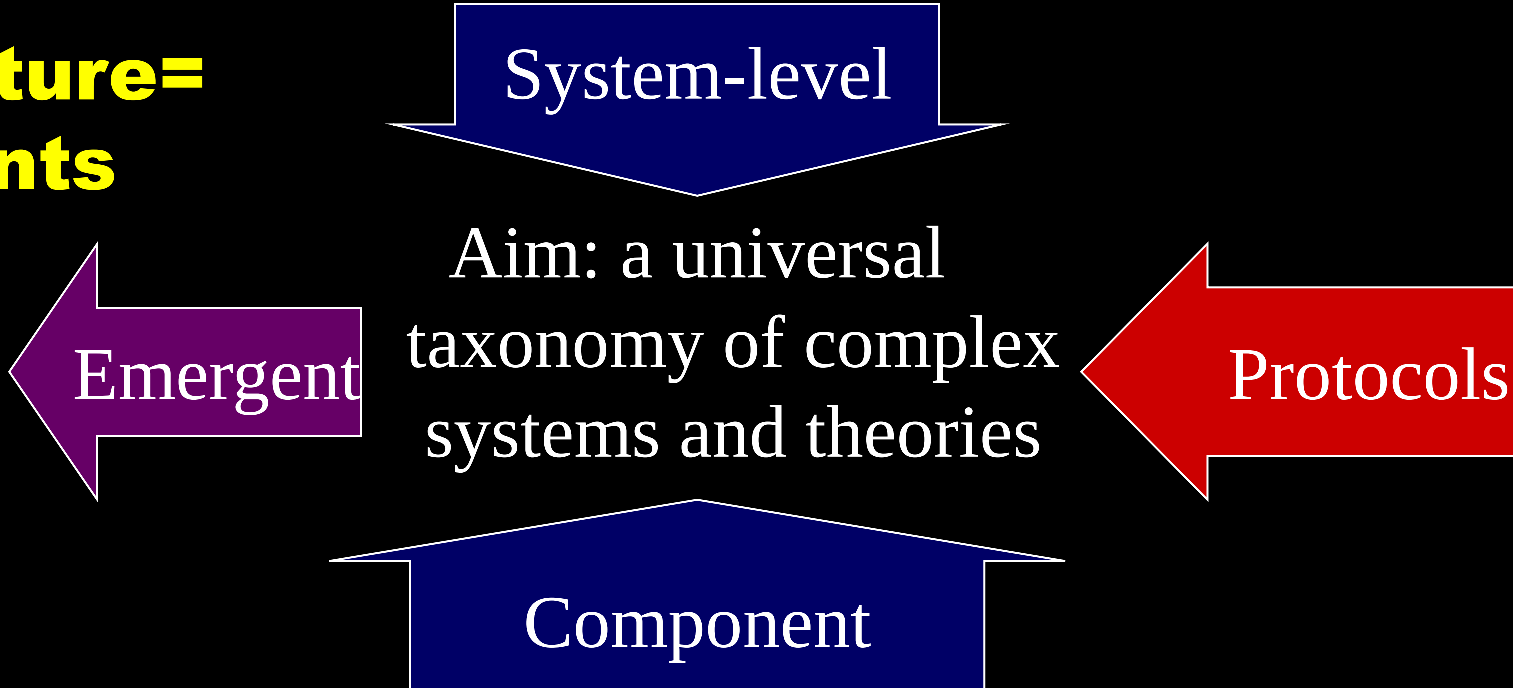
We will take horizontal and vertical slices through biology to illustrate the essentials.



We need to look at the entire biosphere.

An understanding of architecture is essential to making any sense of this.

Architecture= Constraints

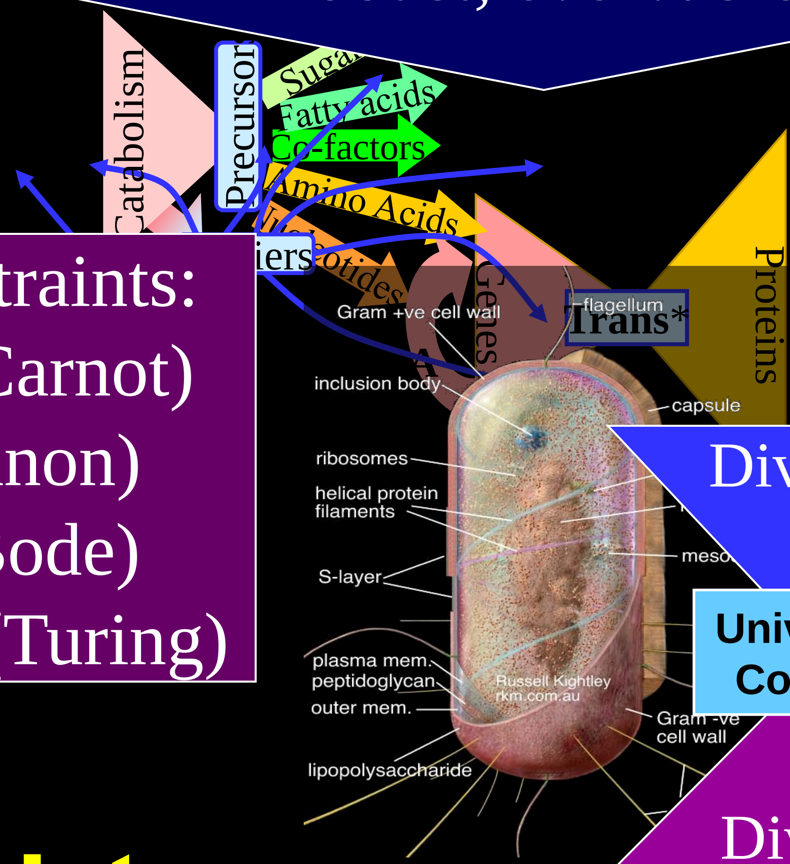


- Describe systems/components in terms of constraints on what is possible
- Decompose constraints into component, system-level, protocols, and emergent
- Not necessarily unique, but hopefully illuminating nonetheless

Systems requirements: functional, efficient, robust, evolvable

Hard constraints:
Thermo (Carnot)
Info (Shannon)
Control (Bode)
Compute (Turing)

Constraints



Diverse

Universal Control

Diverse

Protocols

Components and materials: Energy, moieties

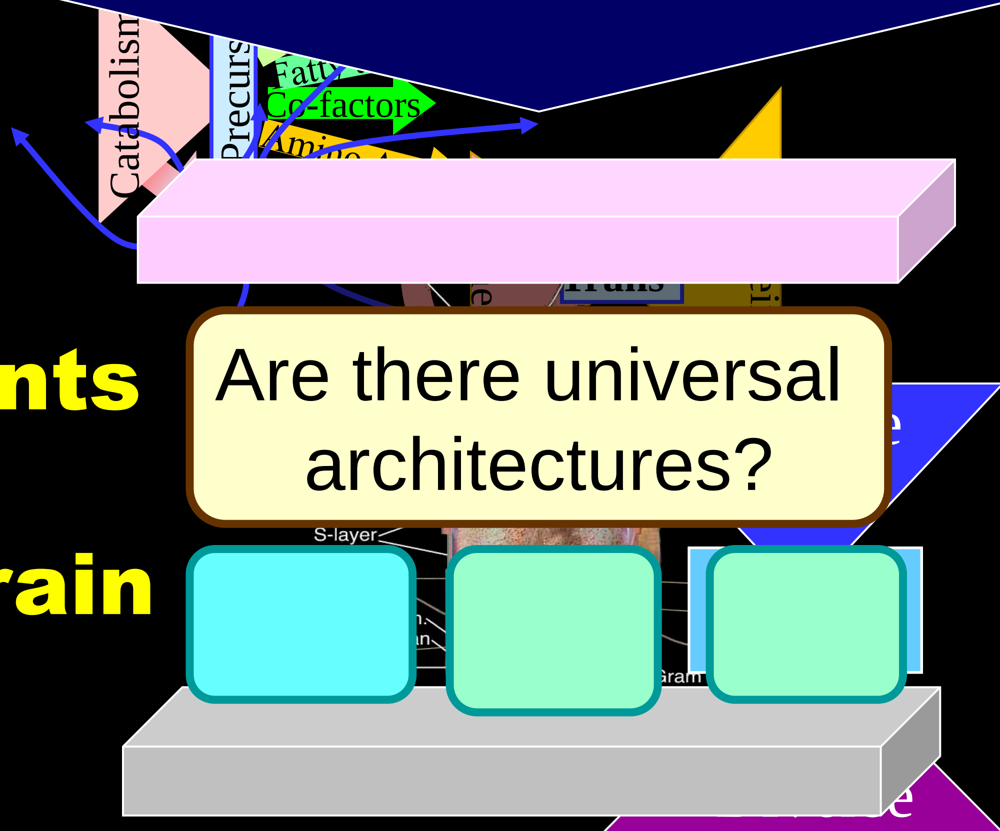
Essential ideas

- Listening to engineers and physicians

- Robust yet fragile (RYF)
- “Constraints that deconstrain” (G&K)

- Network architecture
- Layering
- Control and dynamics (C&D)
- Hourglasses and Bowties
- Unity and diversity

Systems requirements: functional, efficient, robust, evolvable



Constraints that deconstrain

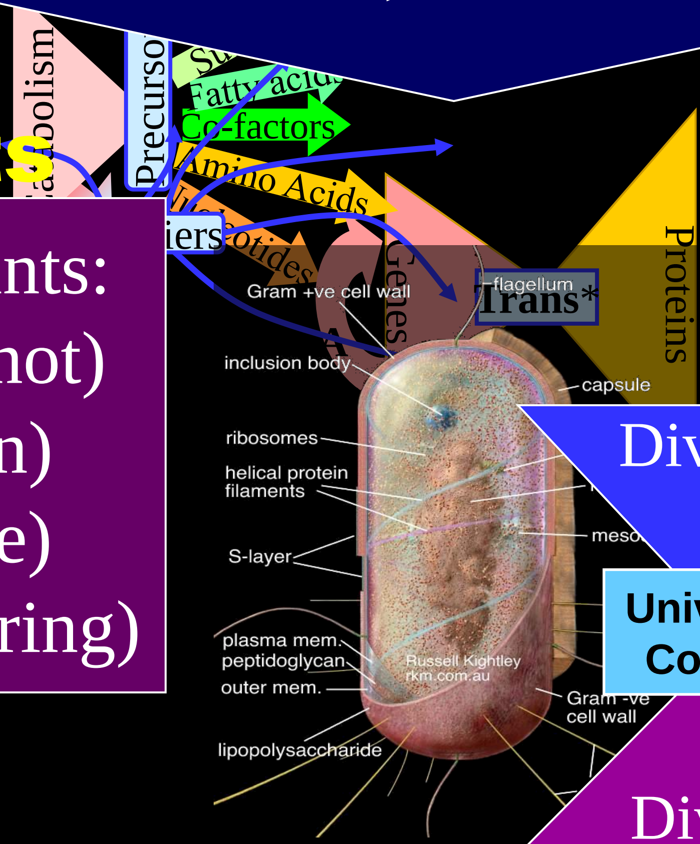
Protocols

Components and materials: Energy, moieties

Systems requirements:
functional, efficient,
robust, evolvable

Emergent Constraints

Hard constraints:
Thermo (Carnot)
Info (Shannon)
Control (Bode)
Compute (Turing)



Diverse

Universal Control

Diverse

Protocols

Components and materials:
Energy, moieties

Are there universal laws?

Emergent Constraints

Hard constraints:
Thermo (Carnot)
Info (Shannon)
Control (Bode)
Compute (Turing)

No networks

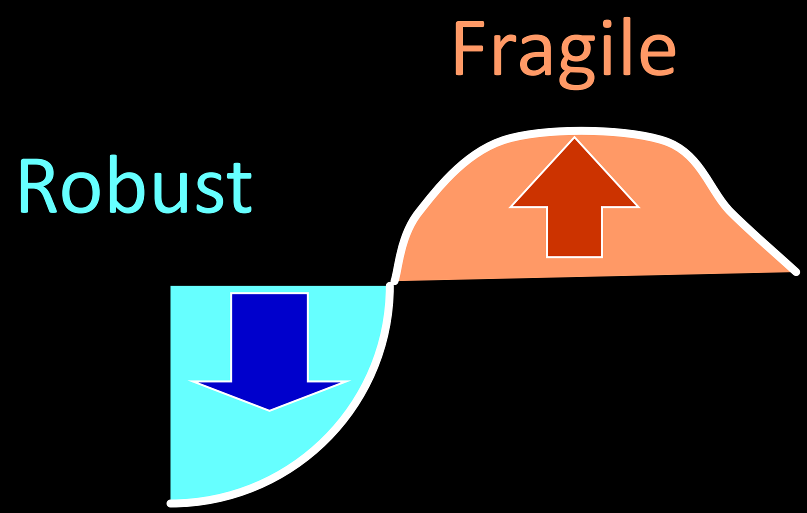
Assume ***different*** architectures a priori.

New unifications are encouraging, but not yet accessible or complete.

Robust Yet Fragile (RYF)

[a system] can have
[a property] ***robust*** for
[a set of perturbations]

Yet be ***fragile*** for
[a different property]
Or [a different perturbation]



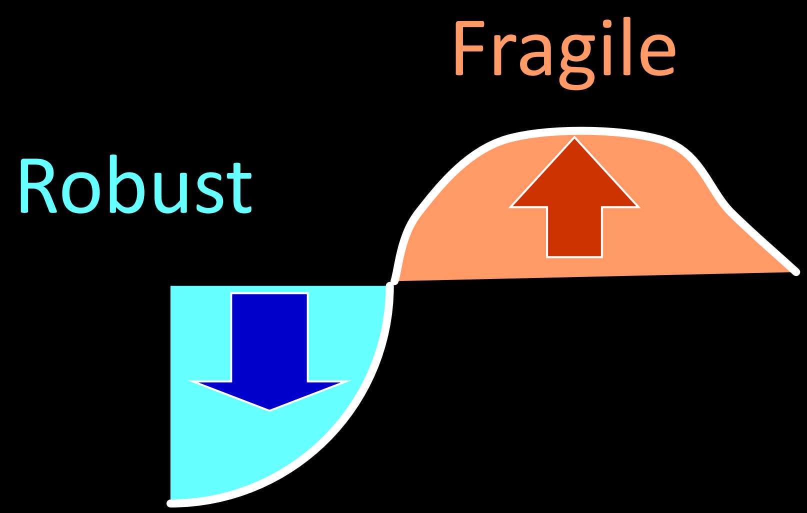
Proposition :
The RYF tradeoff is a ***hard limit*** that cannot be overcome.

Cyber

- Thermodynamics
- Communications
- Control
- Computation

Physical

- Thermodynamics
- Communications
- Control
- Computation



<u>Theorems</u> :
RYF tradeoffs are
hard limits

Robust yet fragile

Biology and advanced tech nets show extremes

- Robust Yet Fragile
- Simplicity and complexity
- Unity and diversity
- Evolvable and frozen

What makes this possible and/ or inevitable?

Architecture (= constraints)

Let’s dig deeper.

More details in applications

We'd need to look at an entire industry.

More details about the hardware design and supply chain

An understanding of architecture is essential to making any sense of this.

Is there a simpler example than Internet?

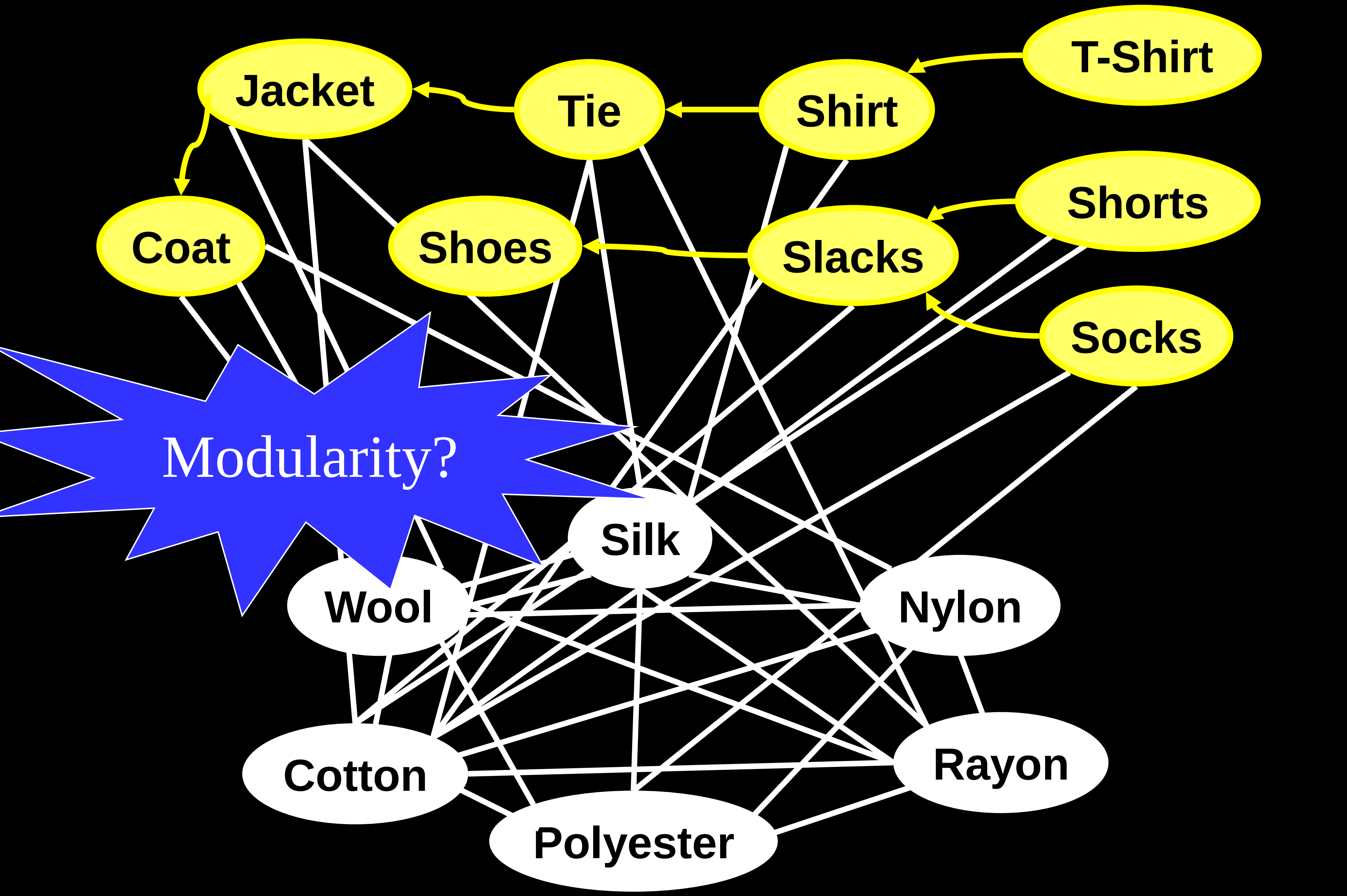
$\exists$ devil $\in$ details

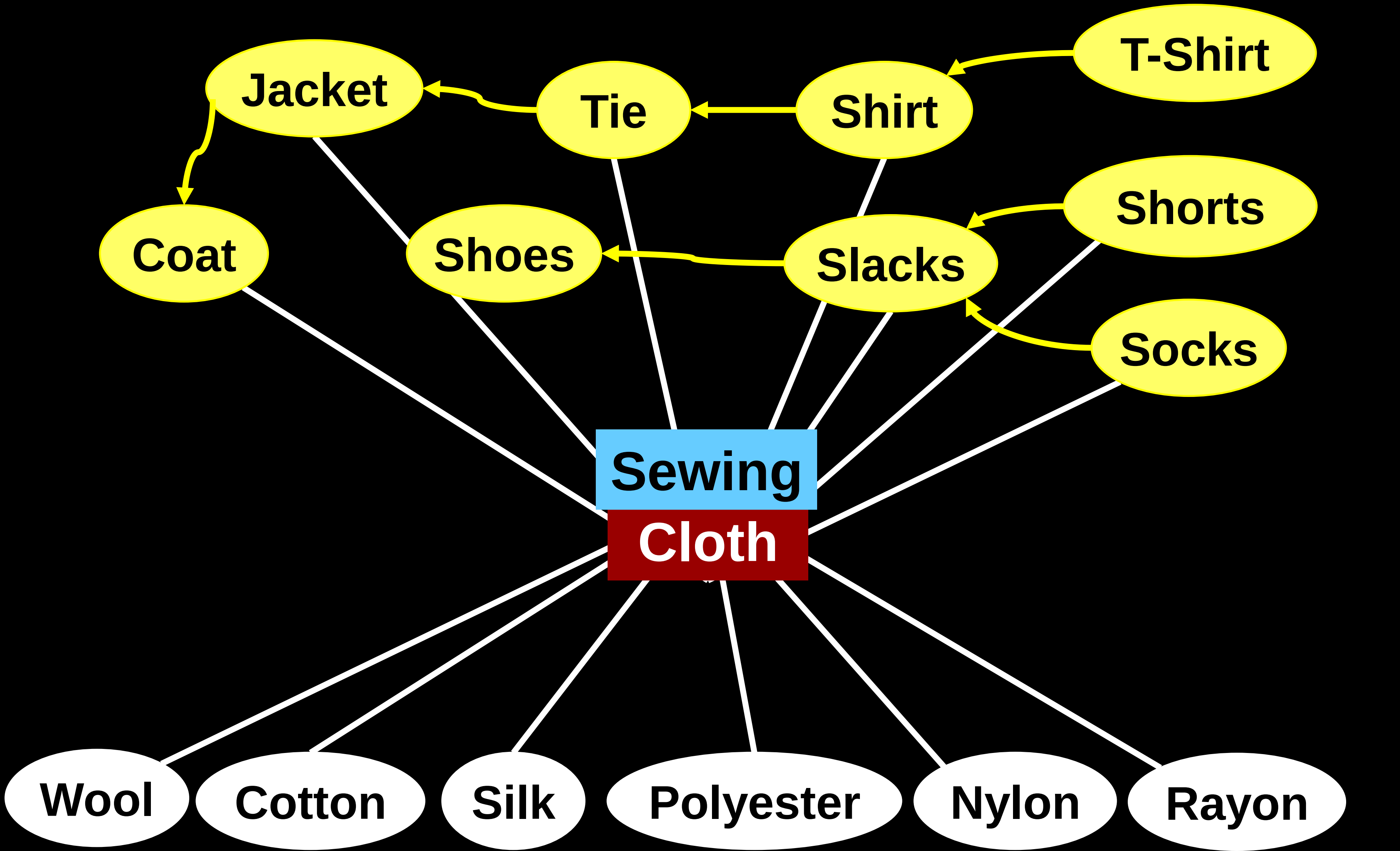
$\Rightarrow$ ☹ architecture

Jean Jour (alias John Day)

Other examples

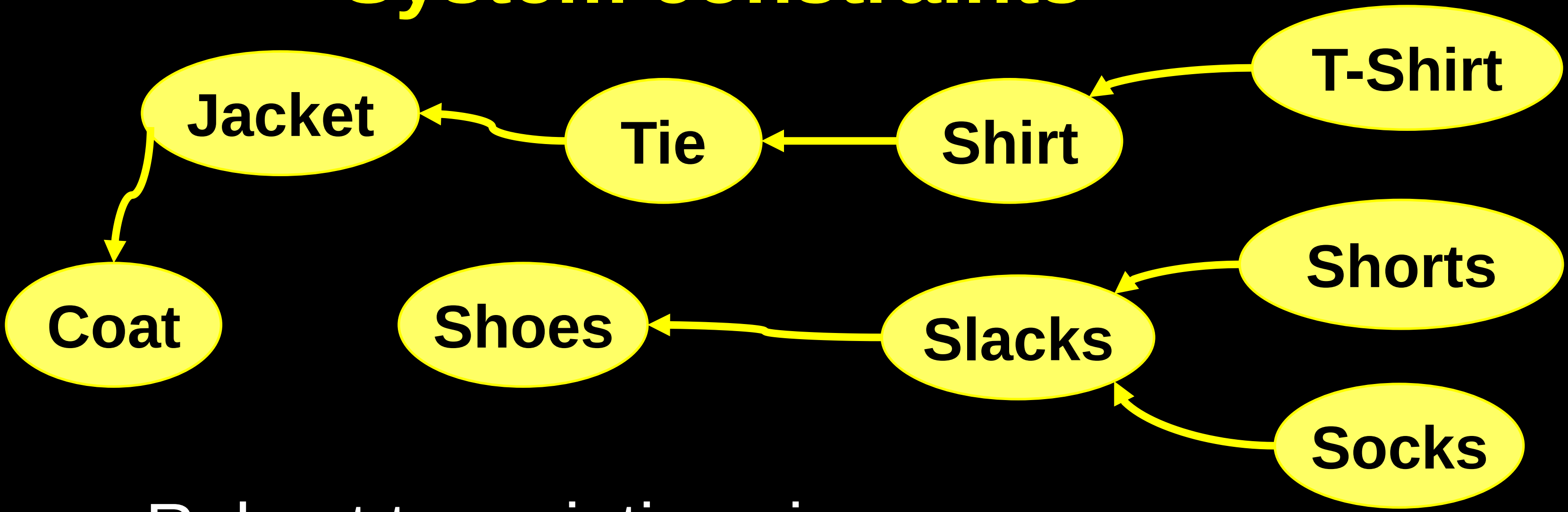
Clothing


T-Shirt
Jacket
Tie
Shirt
Shorts
Coat
Shoes
Slacks
Socks
Modularity?
Silk
Wool
Nylon
Cotton
Rayon
Polyester



T-Shirt
Jacket
Tie
Shirt
Shorts
Coat
Shoes
Slacks
Socks
Sewing
Cloth
Wool
Cotton
Silk
Polyester
Nylon
Rayon

System constraints



Robust to variations in

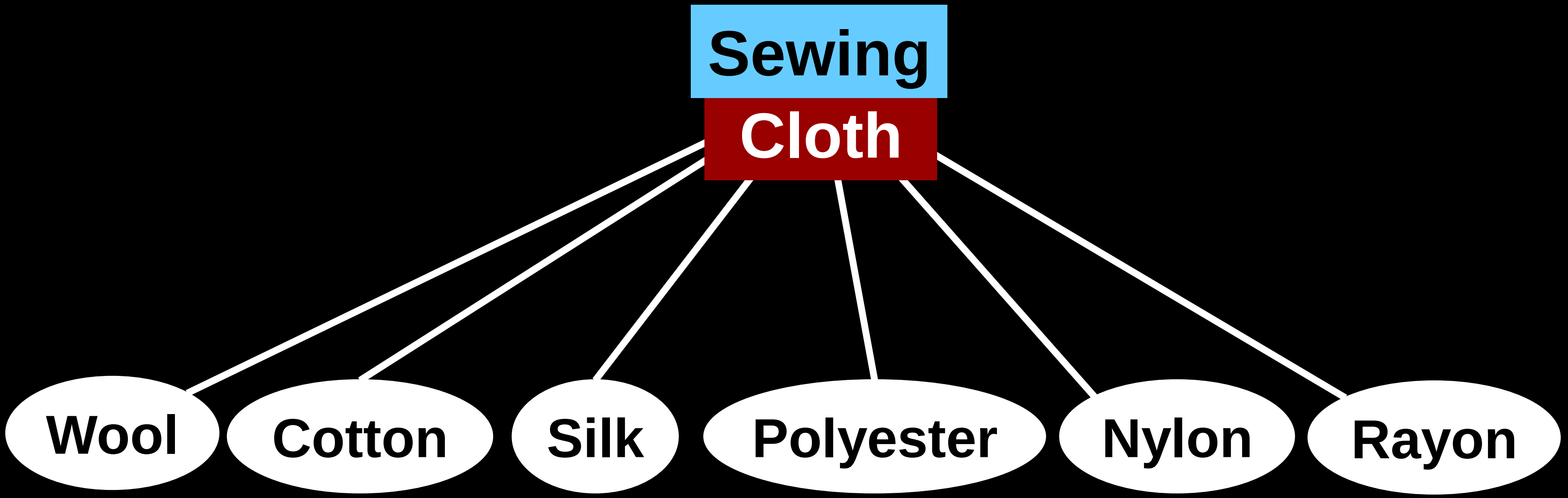
- weather
- activity
- appearance requirements
- wear and tear
- cleaning

Wool Cotton Silk Polyester Nylon Rayon

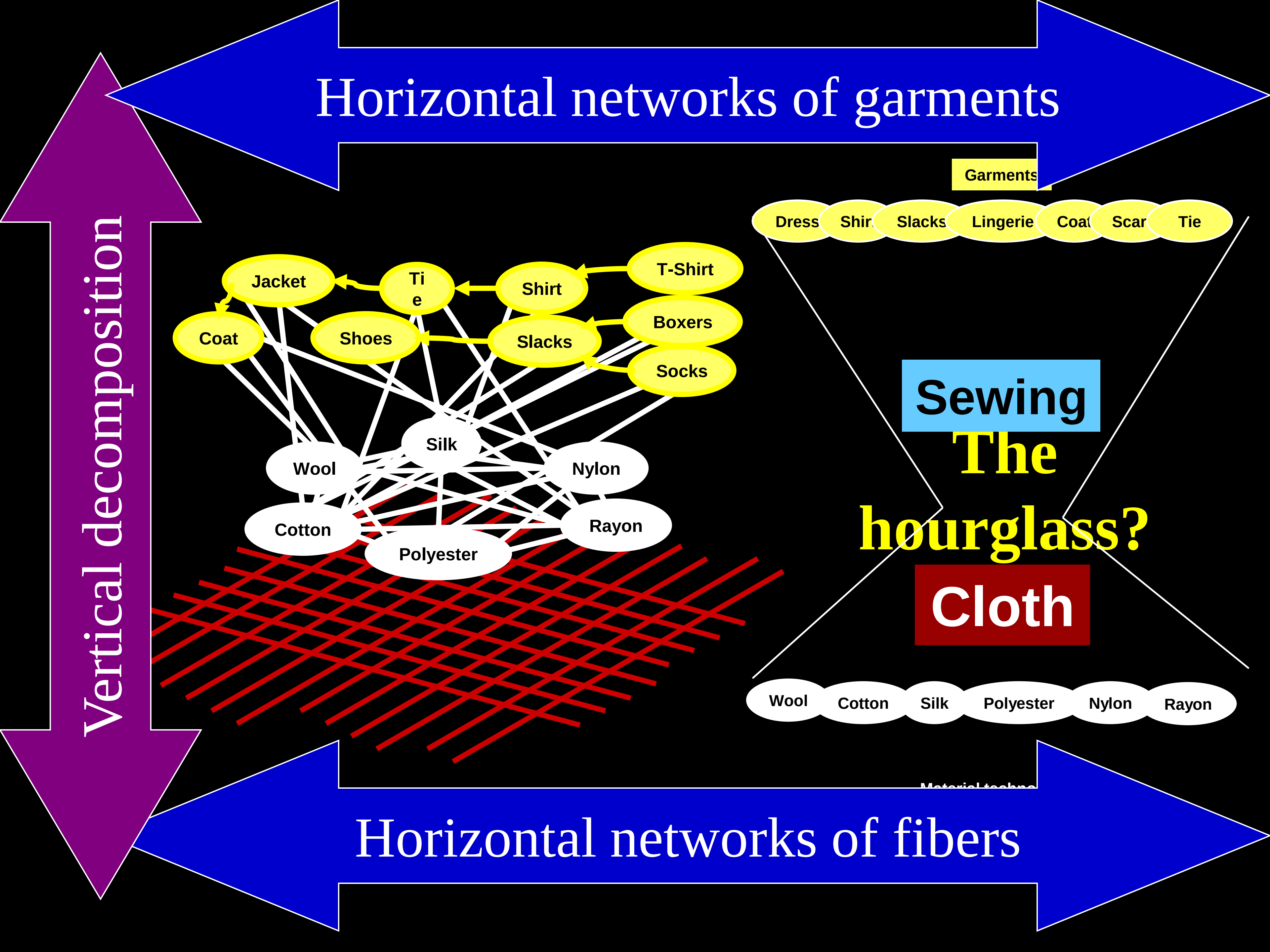
Component constraints

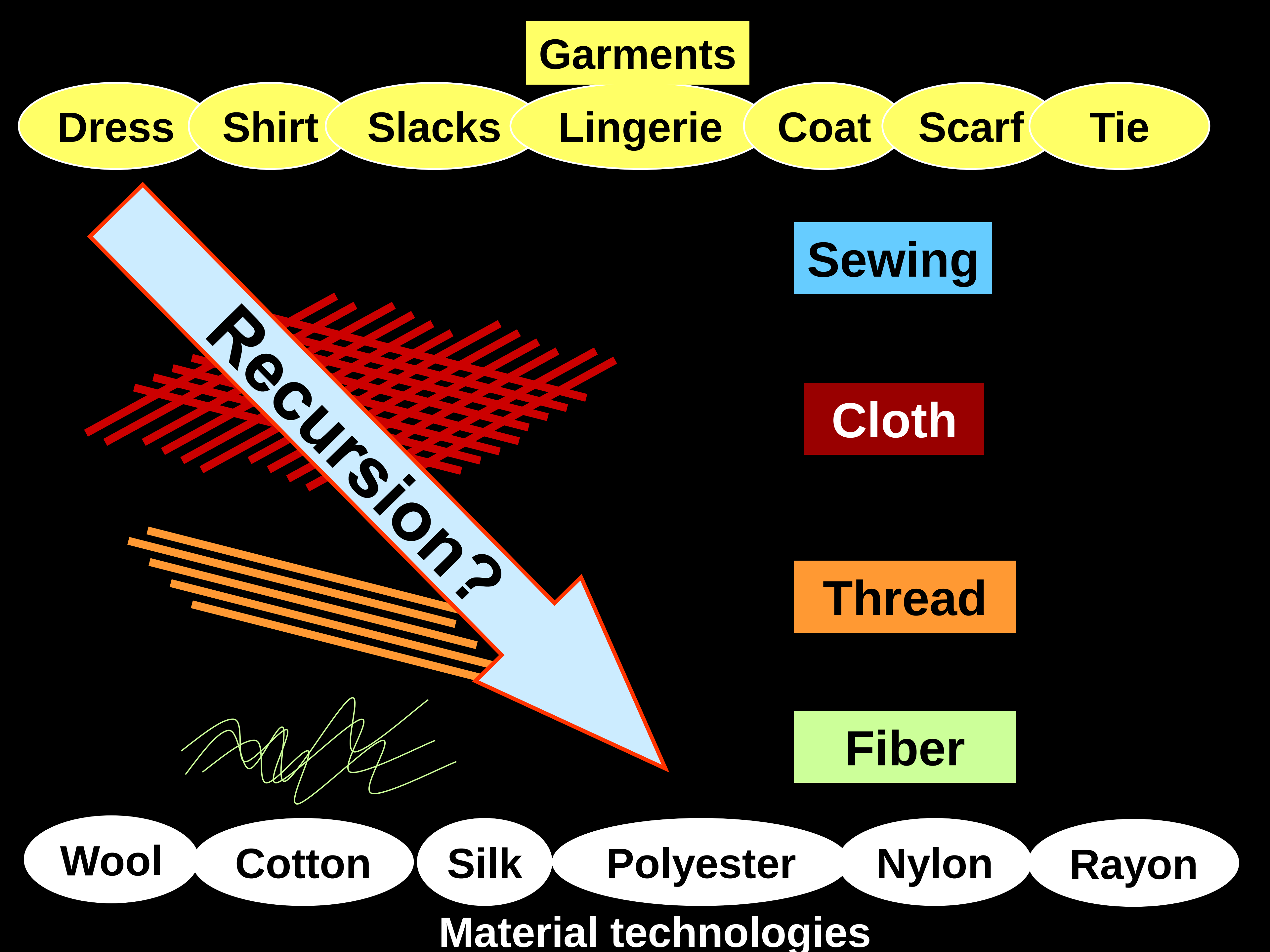
Robust to

- perturbations to clothing
- variety of raw materials
- ***unraveling***

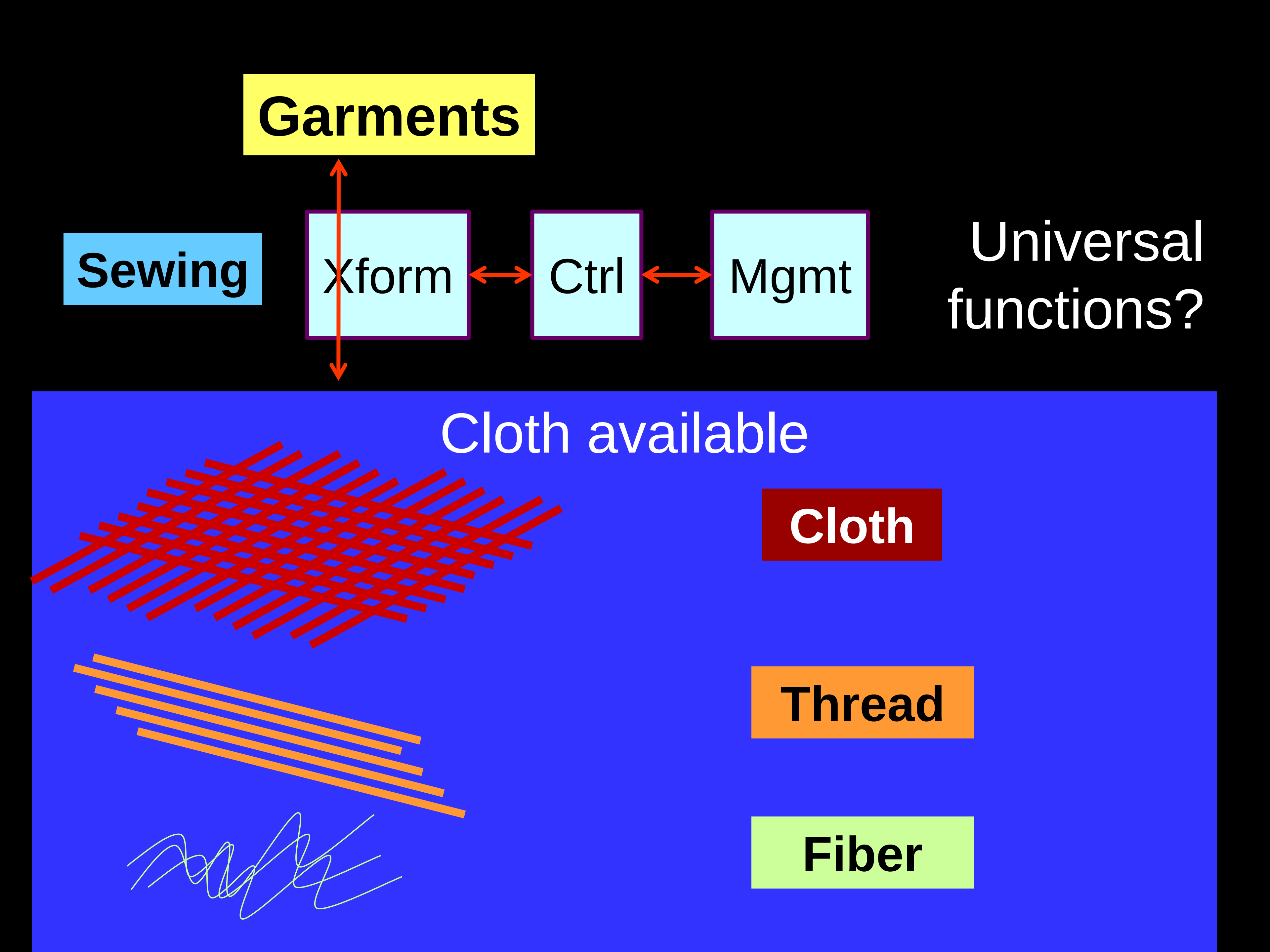


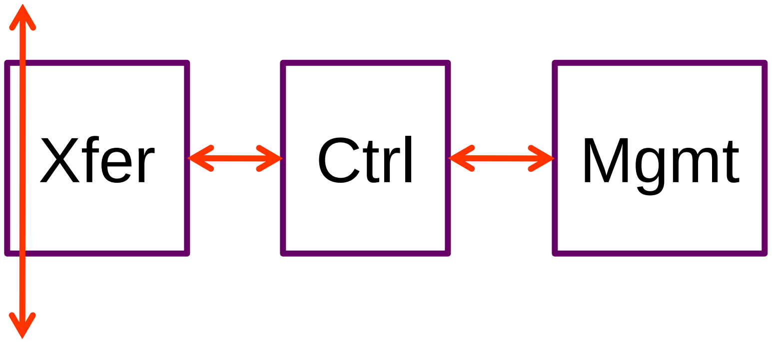
Component constraints


Horizontal networks of garments
Vertical decomposition
Garments
Dress
Shir
Slacks
Lingerie
Coat
Scar
Tie
Jacket
Ti
e
Shirt
T-Shirt
Coat
Shoes
Slacks
Boxers
Socks
Silk
Wool
Nylon
Cotton
Rayon
Polyester
Sewing
The
hourglass?
Cloth
Wool
Cotton
Silk
Polyester
Nylon
Rayon
Horizontal networks of fibers



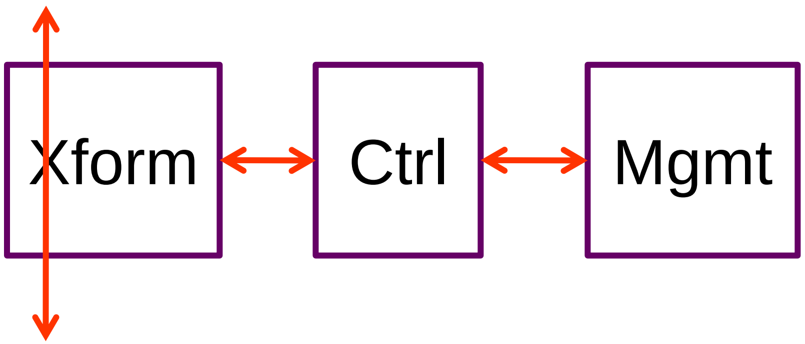
Garments
Dress
Shirt
Slacks
Lingerie
Coat
Scarf
Tie
Recursion?
Sewing
Cloth
Thread
Fiber
Wool
Cotton
Silk
Polyester
Nylon
Rayon
Material technologies


Garments
Sewing
Xform
Ctrl
Mgmt
Universal functions?
Cloth available
Cloth
Thread
Fiber



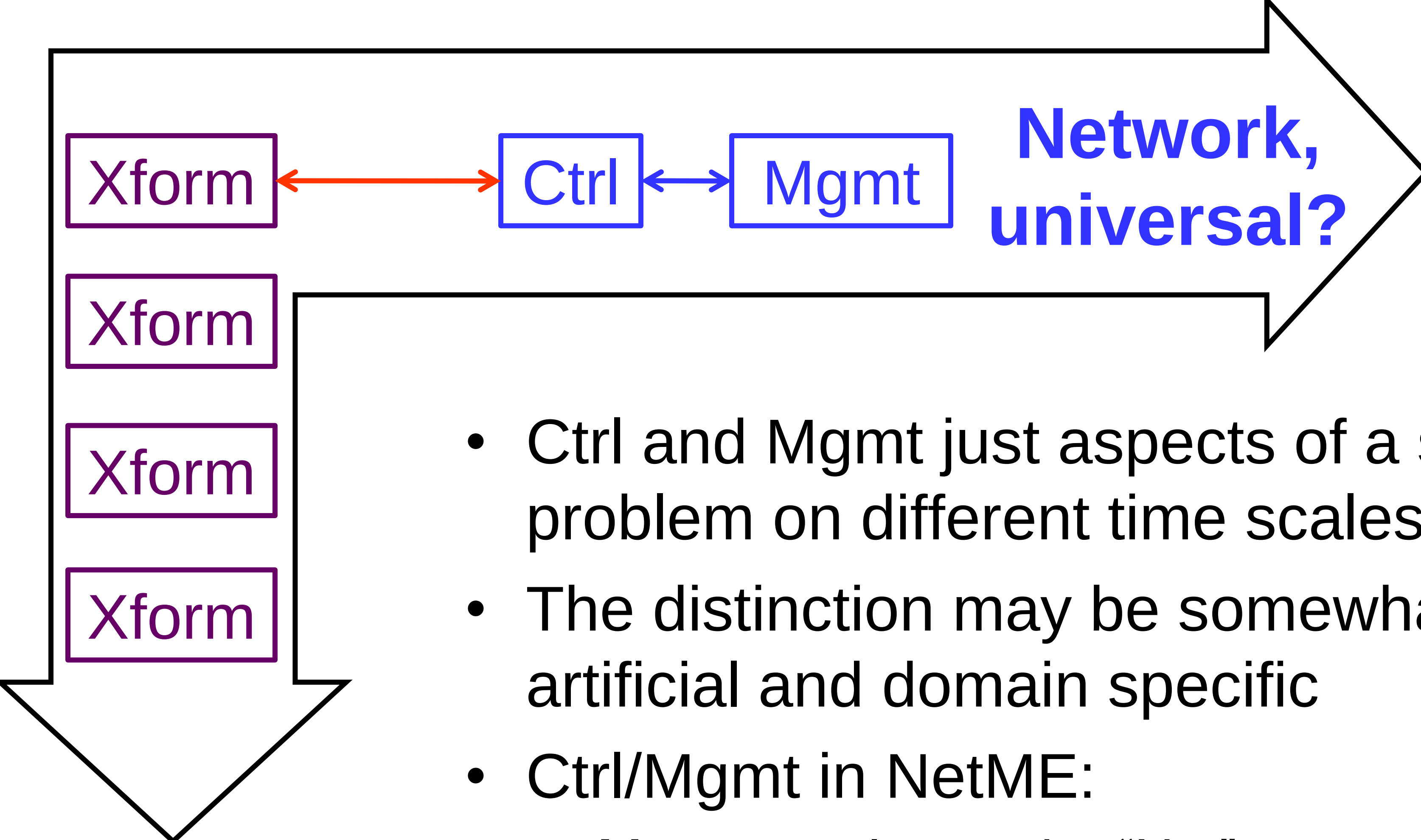
Universal functions?

- Transfer or transform (fastest)
  - **Domain specific (data, power, goods, etc)**
  - Depends on demand and supply
- Control (middle)
  - Schedule/MUX resources in time and space
  - Flow and error control
- Management (slowest)
  - ***What*** resources are available?
  - ***Where*** are they?
  - Cost? Risk? etc



Sewing function?

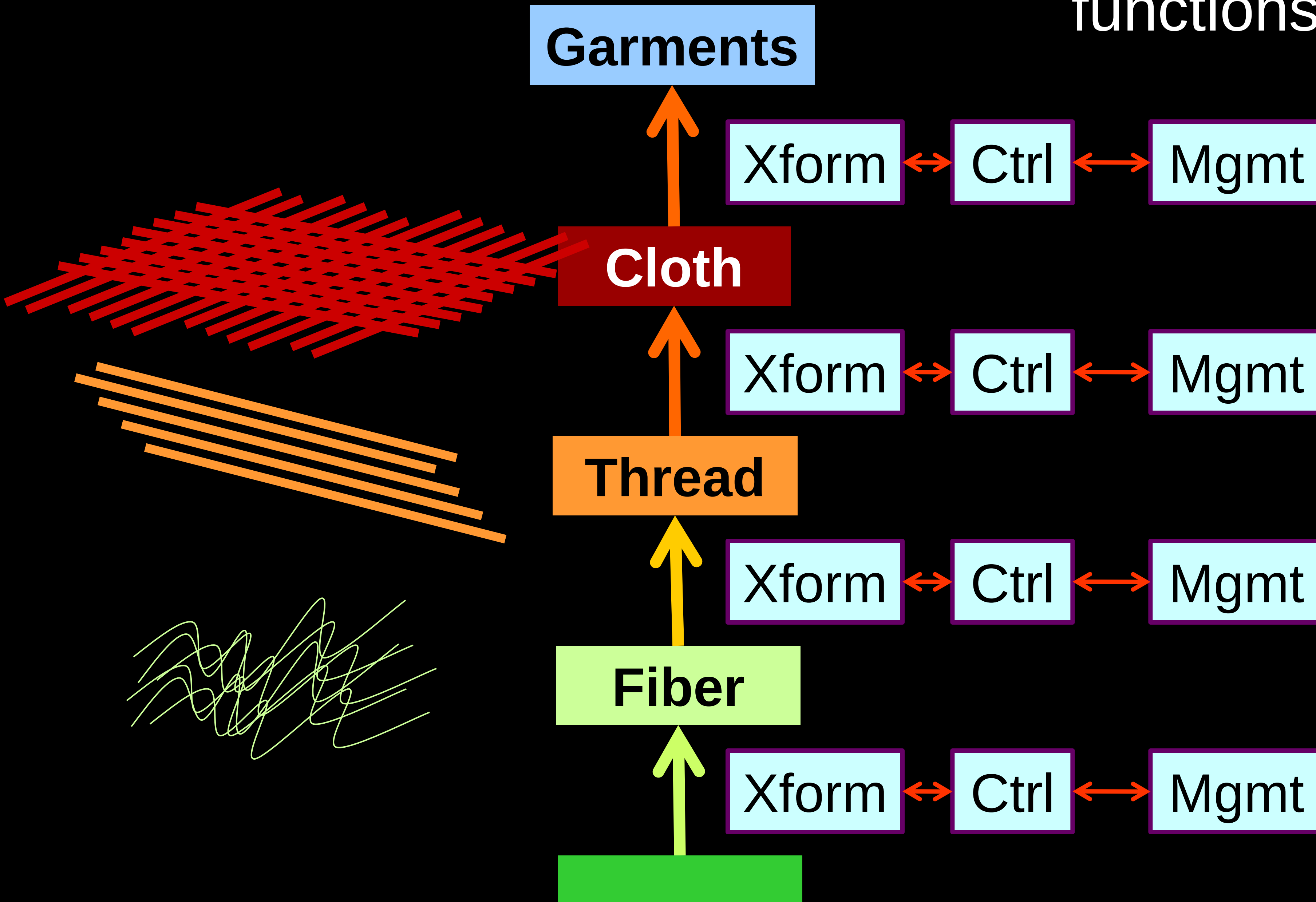
- Transfer or transform (fastest)
  - **Transform cloth to garments**
  - Depends on demand and supply
- Control (middle)
  - Schedule/MUX resources in time and space
  - Flow and error control
- Management (slowest)
  - ***What*** resources are available?
  - ***Where*** are they?
  - Cost? Risk? etc

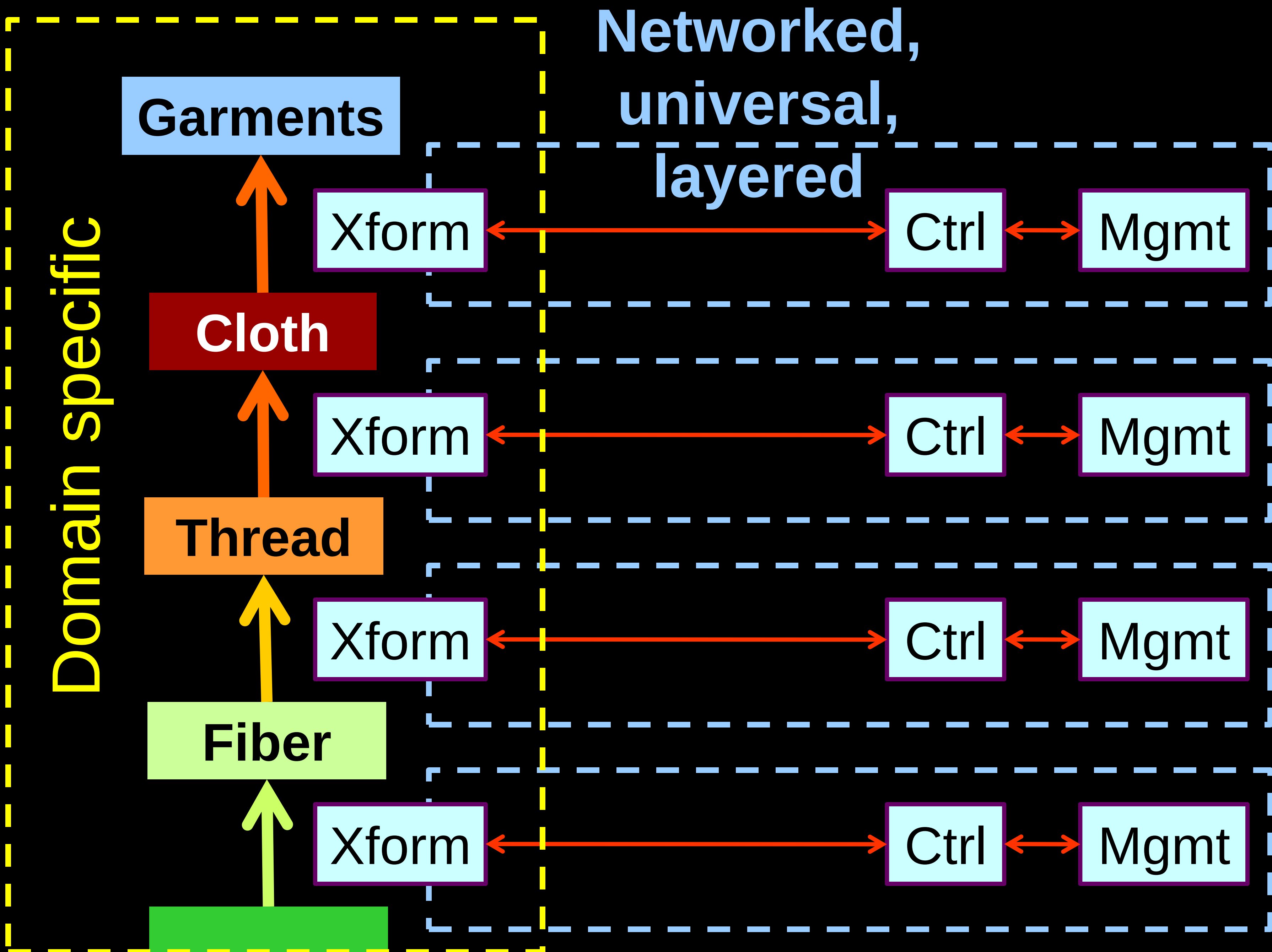


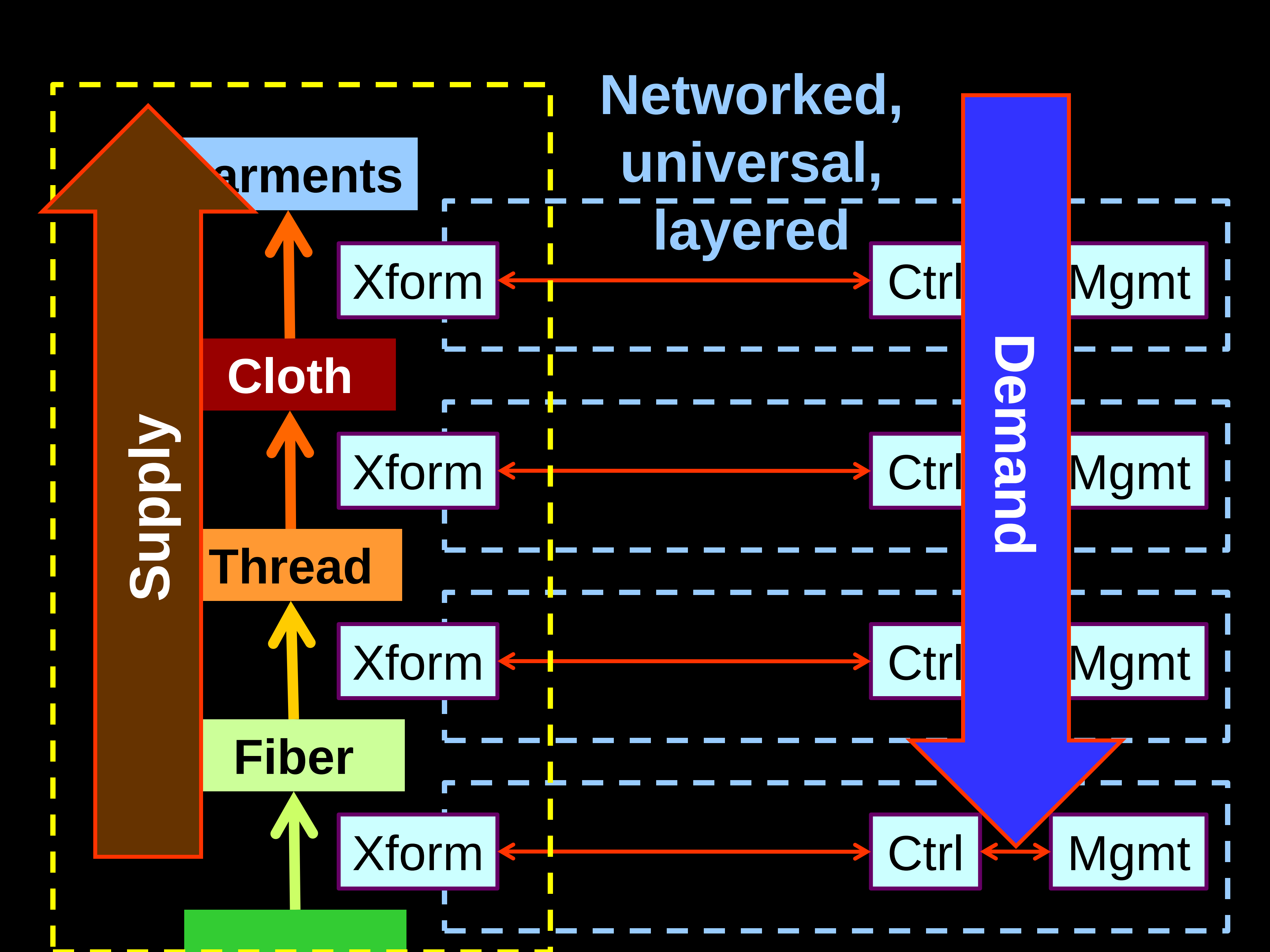
Domain specific, local

- Ctrl and Mgmt just aspects of a single problem on different time scales
- The distinction may be somewhat artificial and domain specific
- Ctrl/Mgmt in NetME:
  - More complex as the "Net" part grows
  - Will be our focus/goal of a unified theory
  - From physics to information to computation to control

Universal functions?

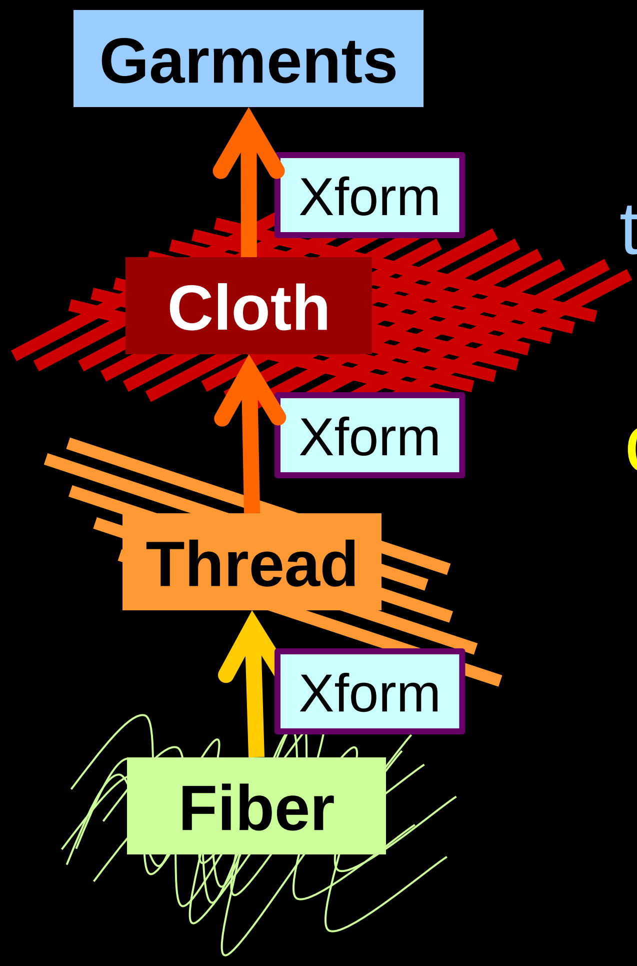



Networked, universal, layered
Domain specific
Garments
Cloth
Thread
Fiber
Xform
Ctrl
Mgmt
Xform
Ctrl
Mgmt
Xform
Ctrl
Mgmt
Xform
Ctrl
Mgmt


Networked,
universal,
layered
Garments
Cloth
Thread
Fiber
Supply
Demand
Xform
Ctrl
Mgmt
Xform
Ctrl
Mgmt
Xform
Ctrl
Mgmt
Xform
Ctrl
Mgmt

Universal strategies?

Even though garments seem analog/continuous



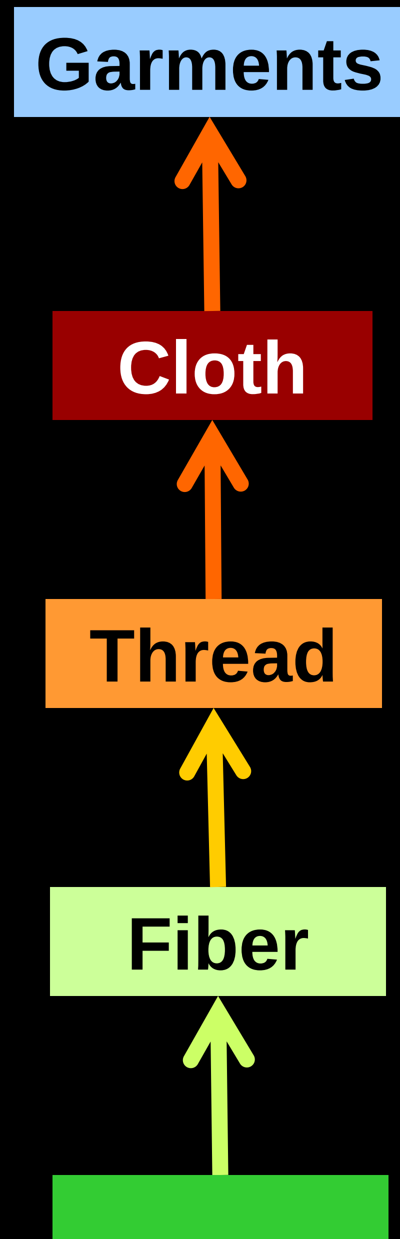
Garments have limited access to threads and fibers

quantization for robustness

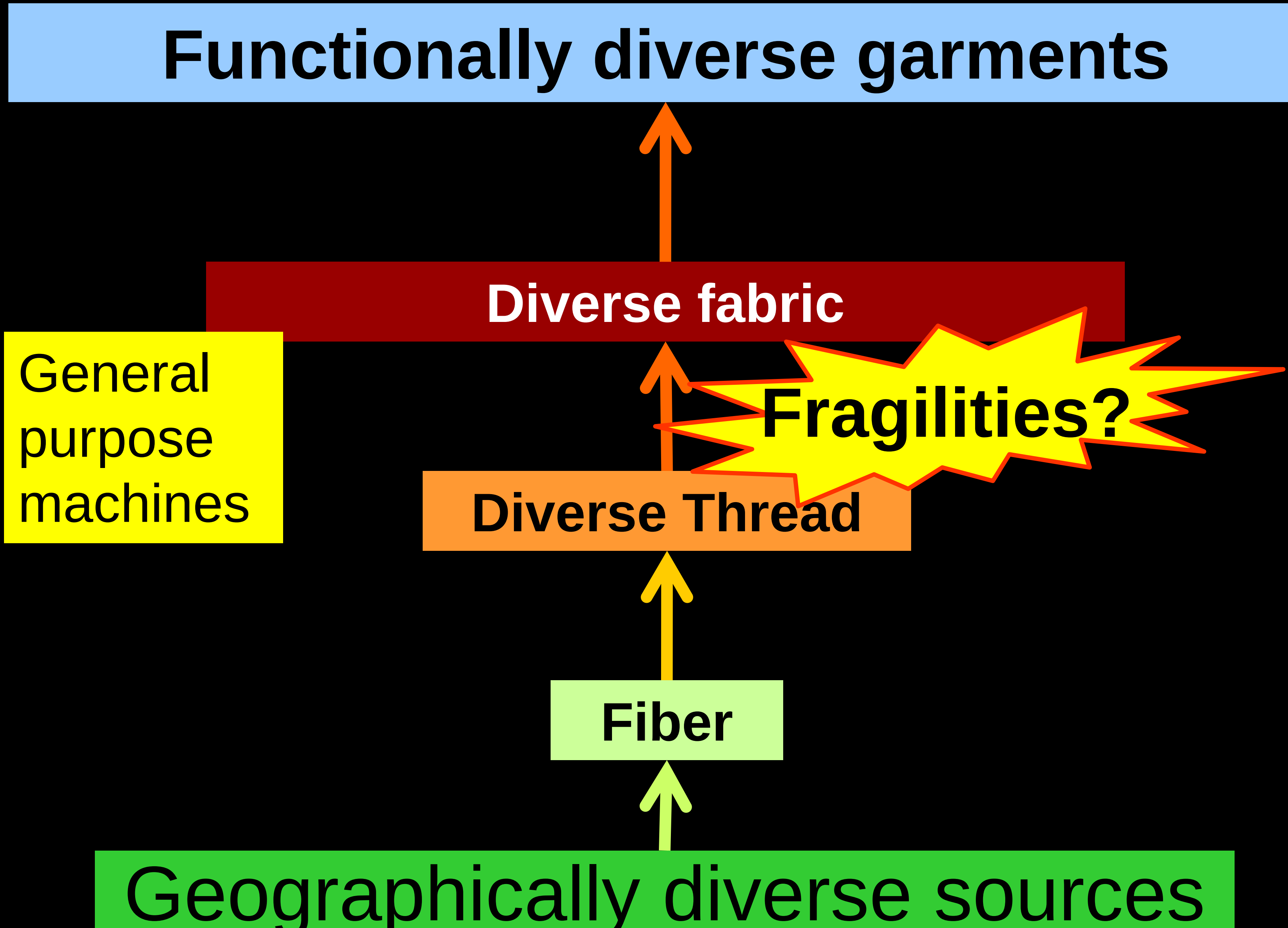
constraints on cross-layer interactions

Prevents unraveling of lower layers

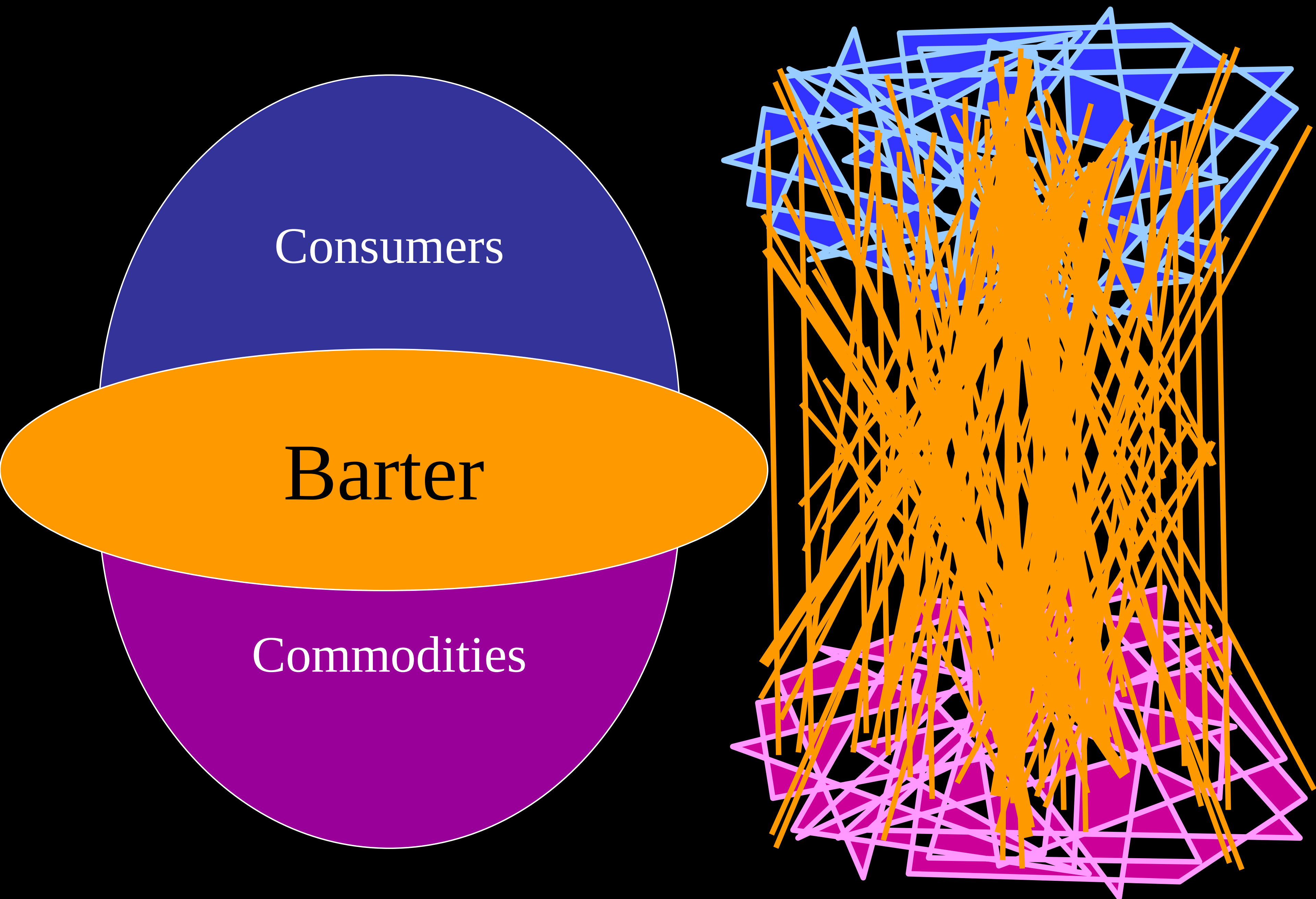
Scalable

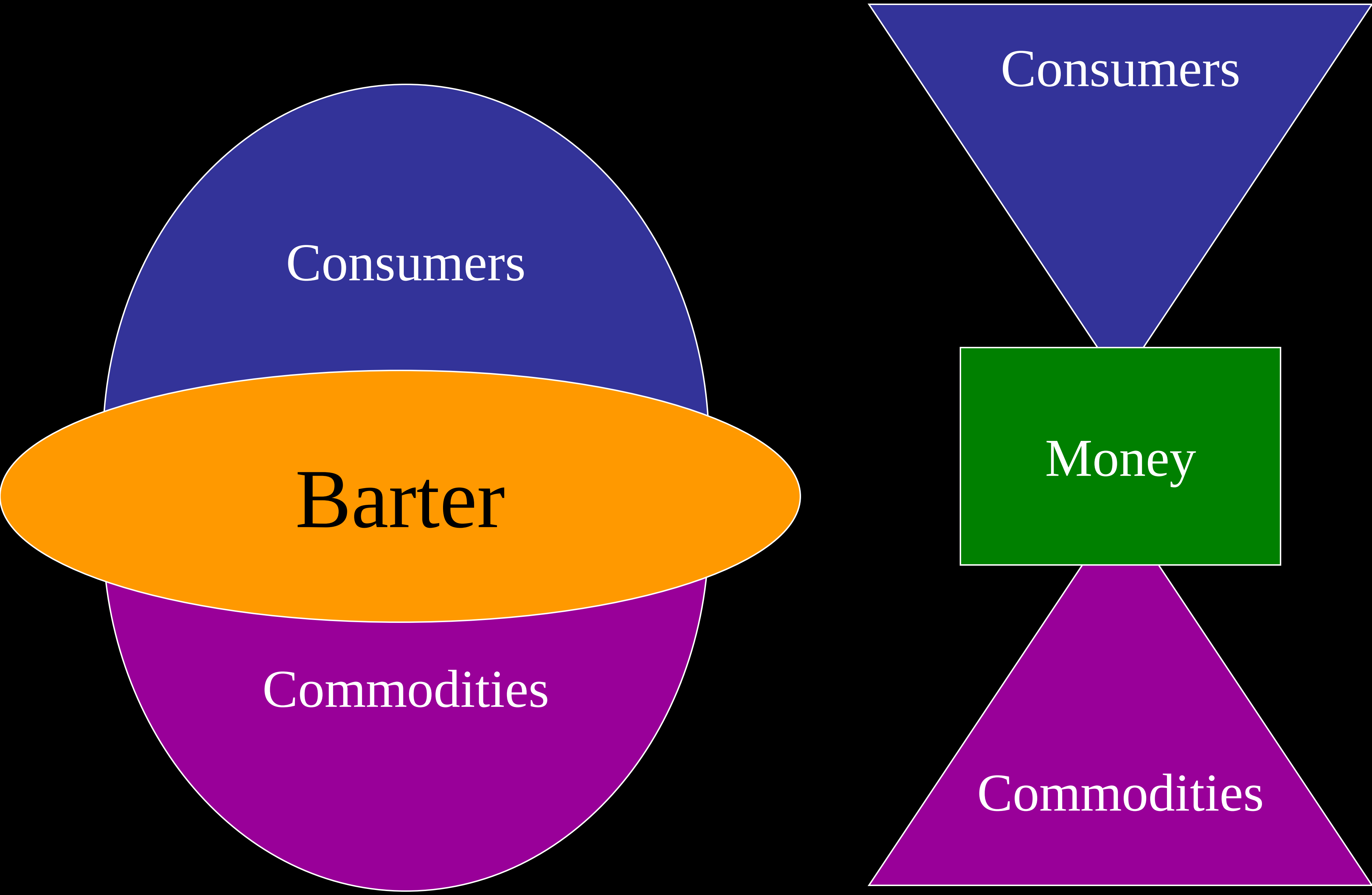


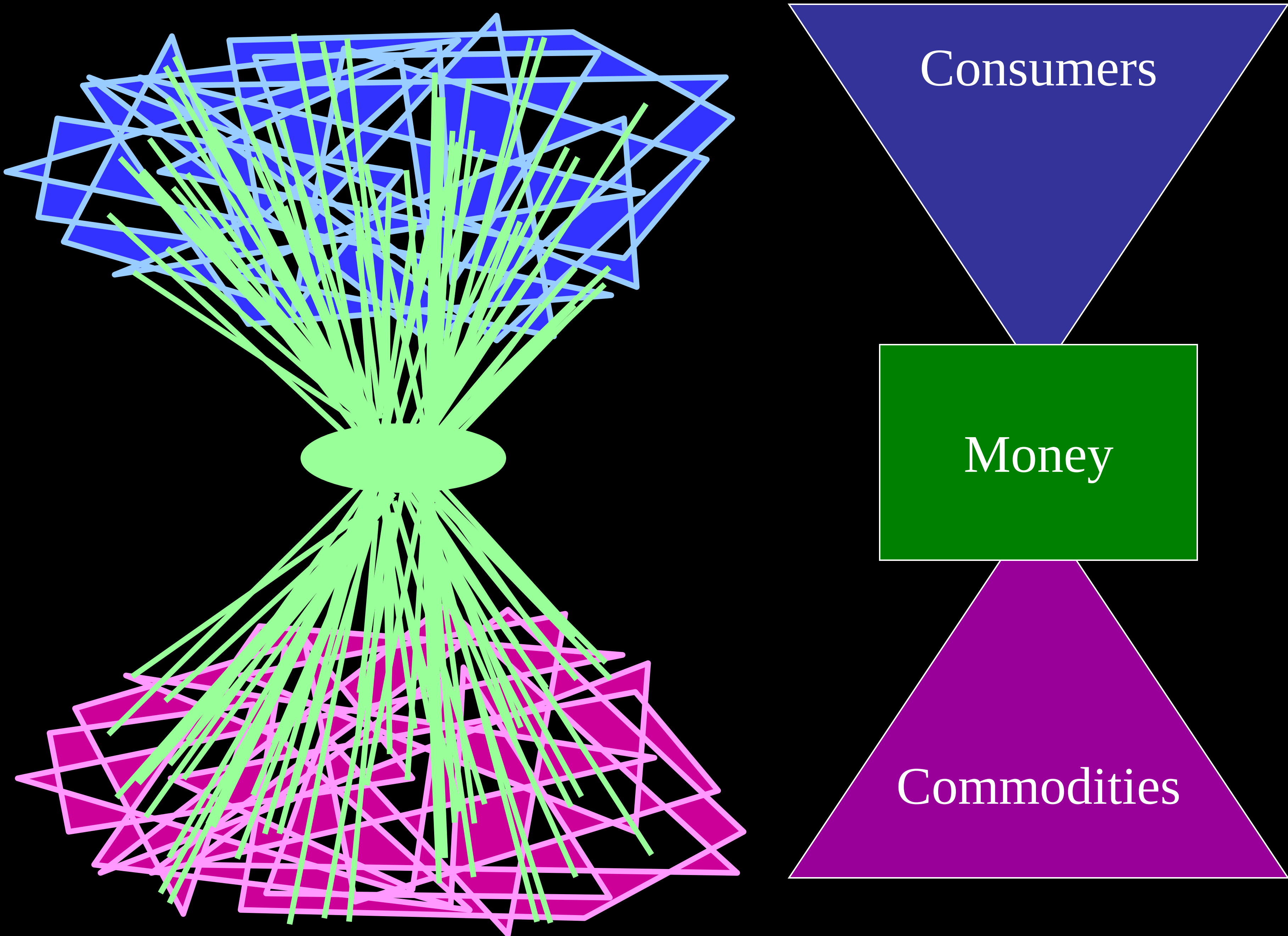
Sustainable?


Functionally diverse garments
Diverse fabric
General purpose machines
Fragilities?
Diverse Thread
Fiber
Geographically diverse sources

Money

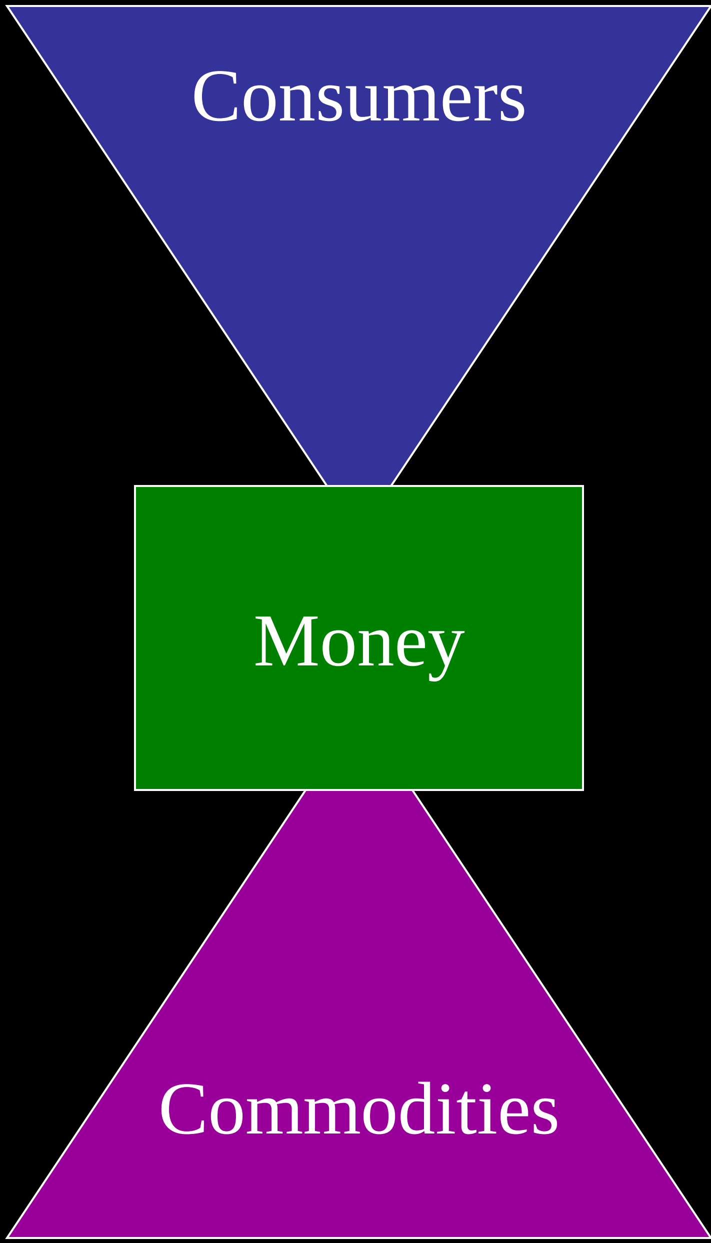

Consumers
Barter
Commodities


Consumers
Barter
Commodities
Consumers
Money
Commodities


Consumers
Money
Commodities

New fragilities

- Theft, counterfeiting, fraud, and “creative accounting” are now possible
- The beginning of a growing complexity-fragility spiral
- Complex legal infrastructure
- Law, banking, finance, Ponzi schemes, derivatives, credit default swaps, …



Lego hourglass

Diverse toys

Universal Control

Diverse instructions

control

assembly

Robust yet fragile

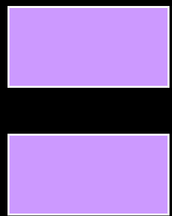
Extremes of

- Robust yet fragile
- Simplicity and complexity
- Constrained and flexible
- Frozen and evolvable
- Digital and analog
- Diverse and conserved

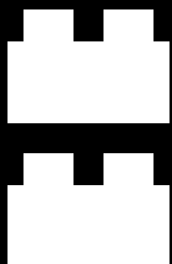
Lego *system* requirements

	Alternative designs?			
Performance				
Trauma				
Allowed connections				
Reuse				
Evolvable parts				
Evolvable systems				
Labor cost				
Parts cost				

Alternatives

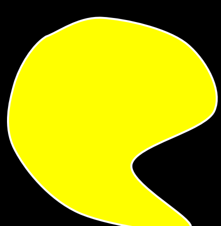


No interface. Simple blocks.



Standard interface. (Wild type.)

Add glue to hold the parts together.



Injection mold the whole toy from scratch.

Lego hourglass

For a single toy

Complexity

control

assembly

Instructions

Analog behavior
Kinematics
Dynamics

Digital description
Control
Assembly

control

Instructions

Toy *system*

Lego hourglass

Huge variety of toys

Standardized mechanisms
Highly conserved

control

assembly

Huge variety of instructions

Instructions

Lego hourglass

Huge variety
of toys

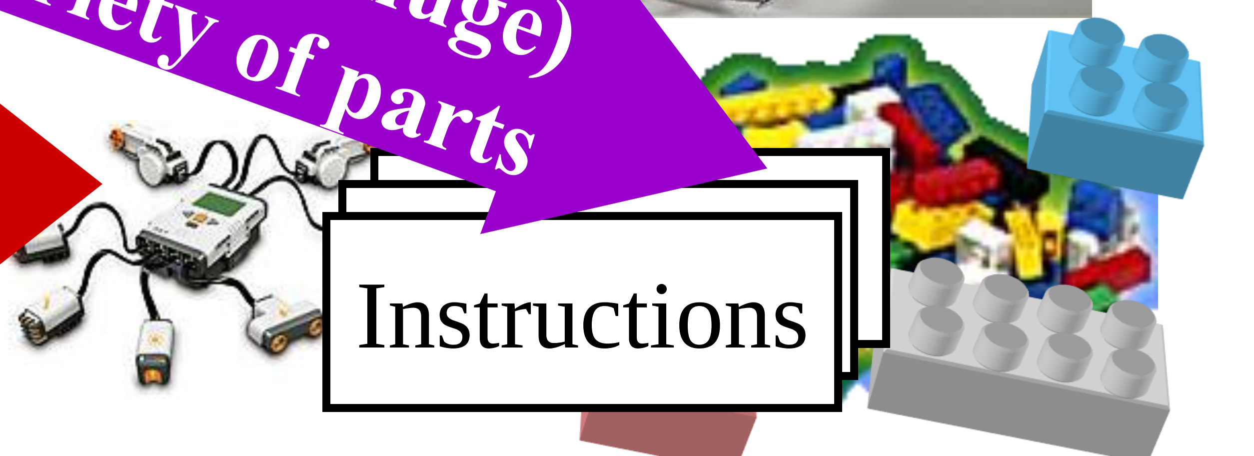
control

Standardized mechanisms
Highly conserv

ssembly

Large (<< huge)
Variety of parts

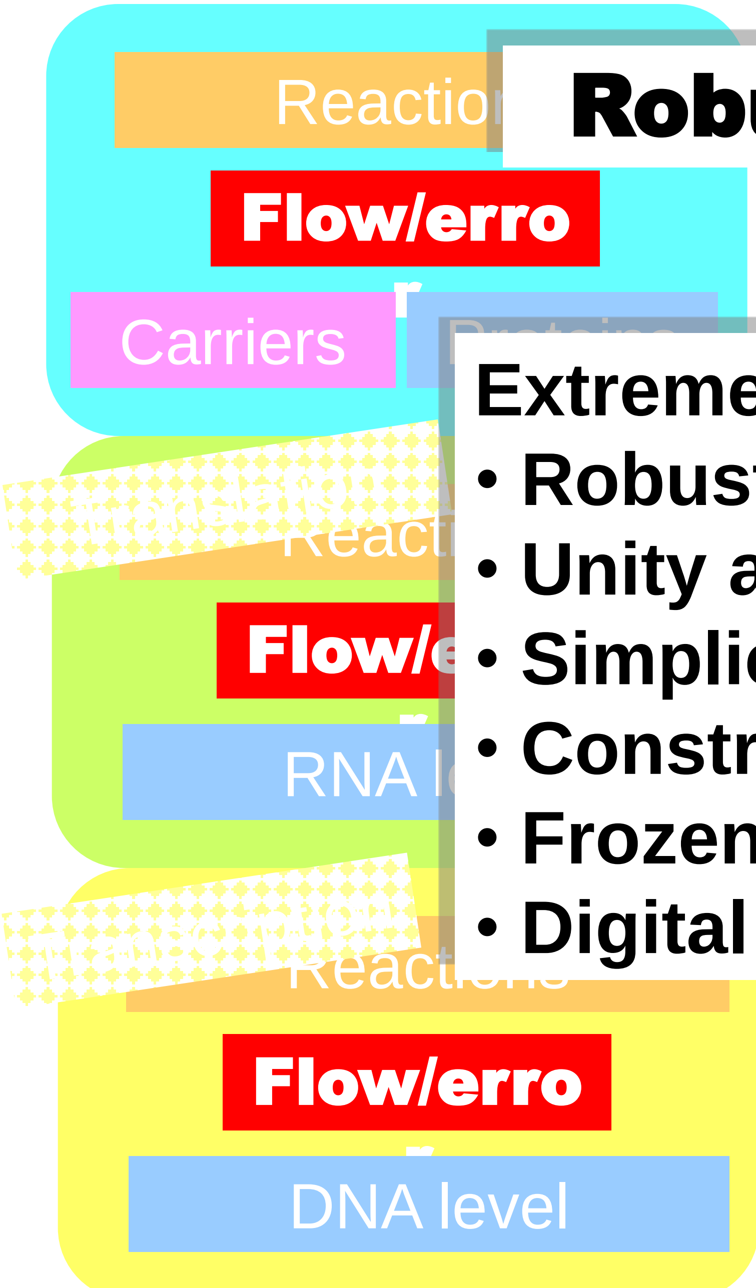
Huge variety
of instructions



Instructions

Robust yet fragile

Extremes of
- Robust yet fragile
- Unity and diversity
- Simplicity and complexity
- Constrained and flexible
- Frozen and evolvable
- Digital and analog



Diverse

Lessons from Lego:

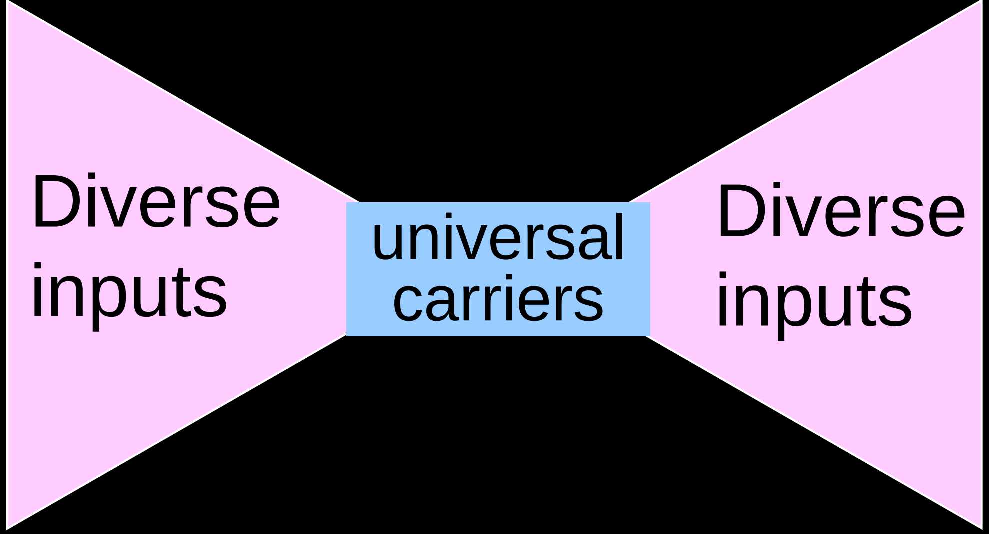
- Infinitely ***diverse*** toys from
- moderately diverse parts
- ***Hourglass*** organization of control
- ***Conserved*** control mechanisms
- ***Bowties*** within layers
- ***Complexity*** is overwhelmingly in conserved control parts, but
- largely hidden in ordinary operation
- Greater internal complexity means more ***robust yet fragile*** external behavior

control

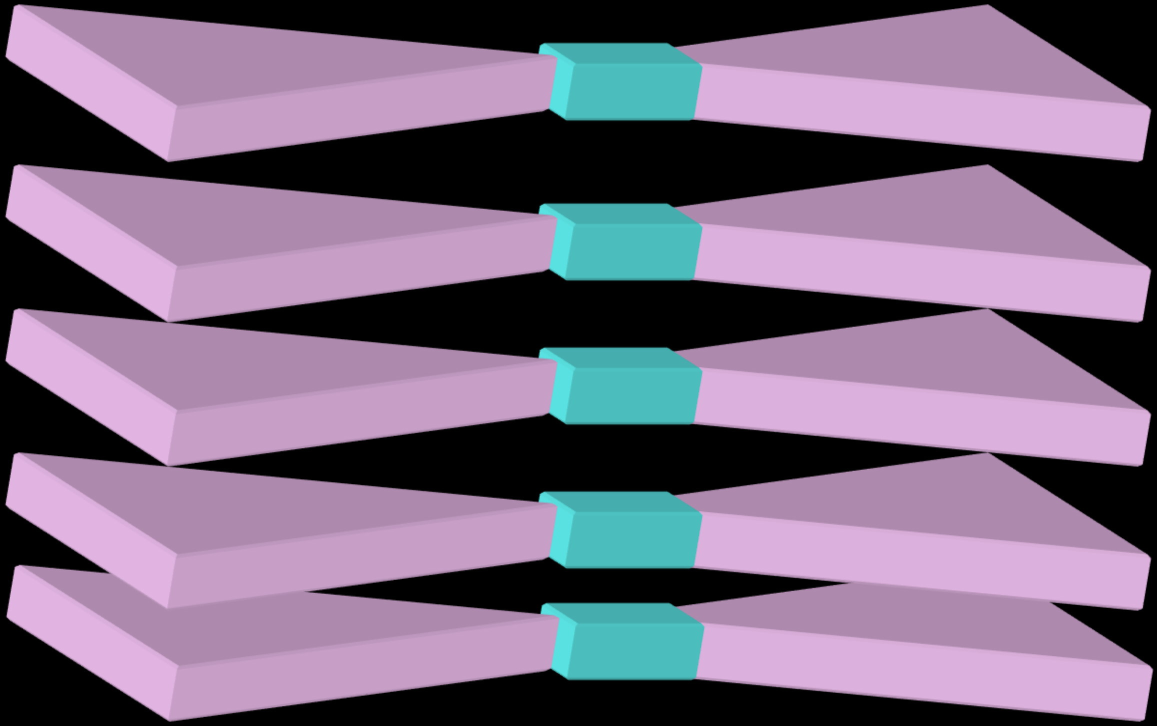
CONSERVED

assembly

Diverse



Layers of bowties



We'll come back to this aspect later.

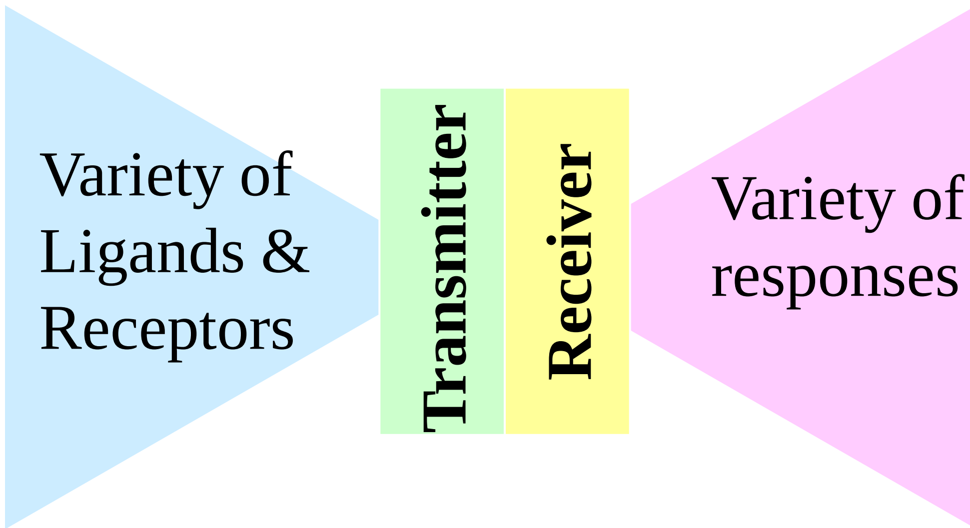
Why bowties?

- Metabolism, biosynthesis, assembly

1. ***Carriers***: Charging carriers in central metabolism
2. ***Precursors***: Biosynthesis of precursors and building blocks
3. ***Trans****: DNA replication, transcription, and translation

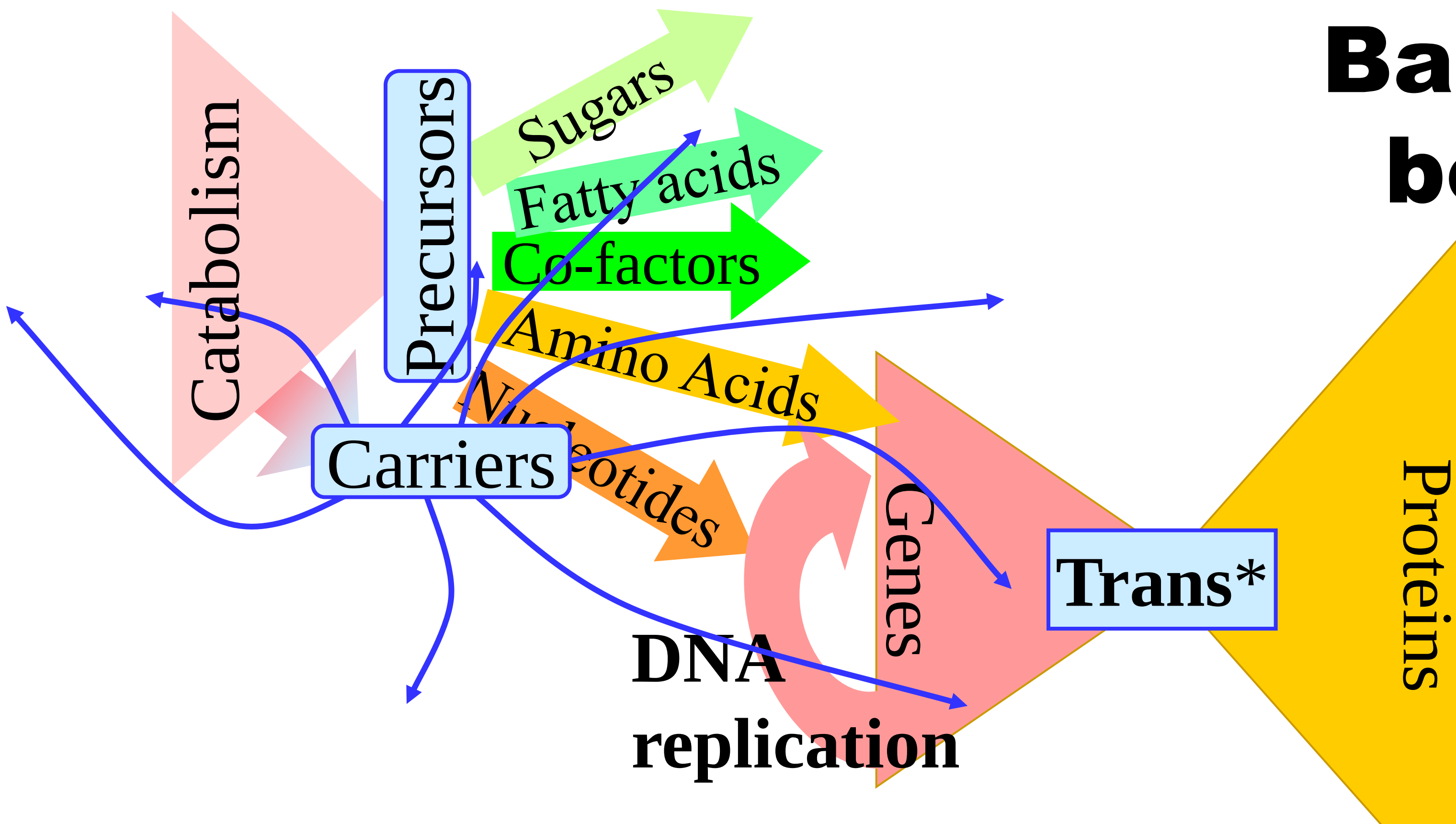
- Signal transduction

4. *2CST*: Two-component signal transduction

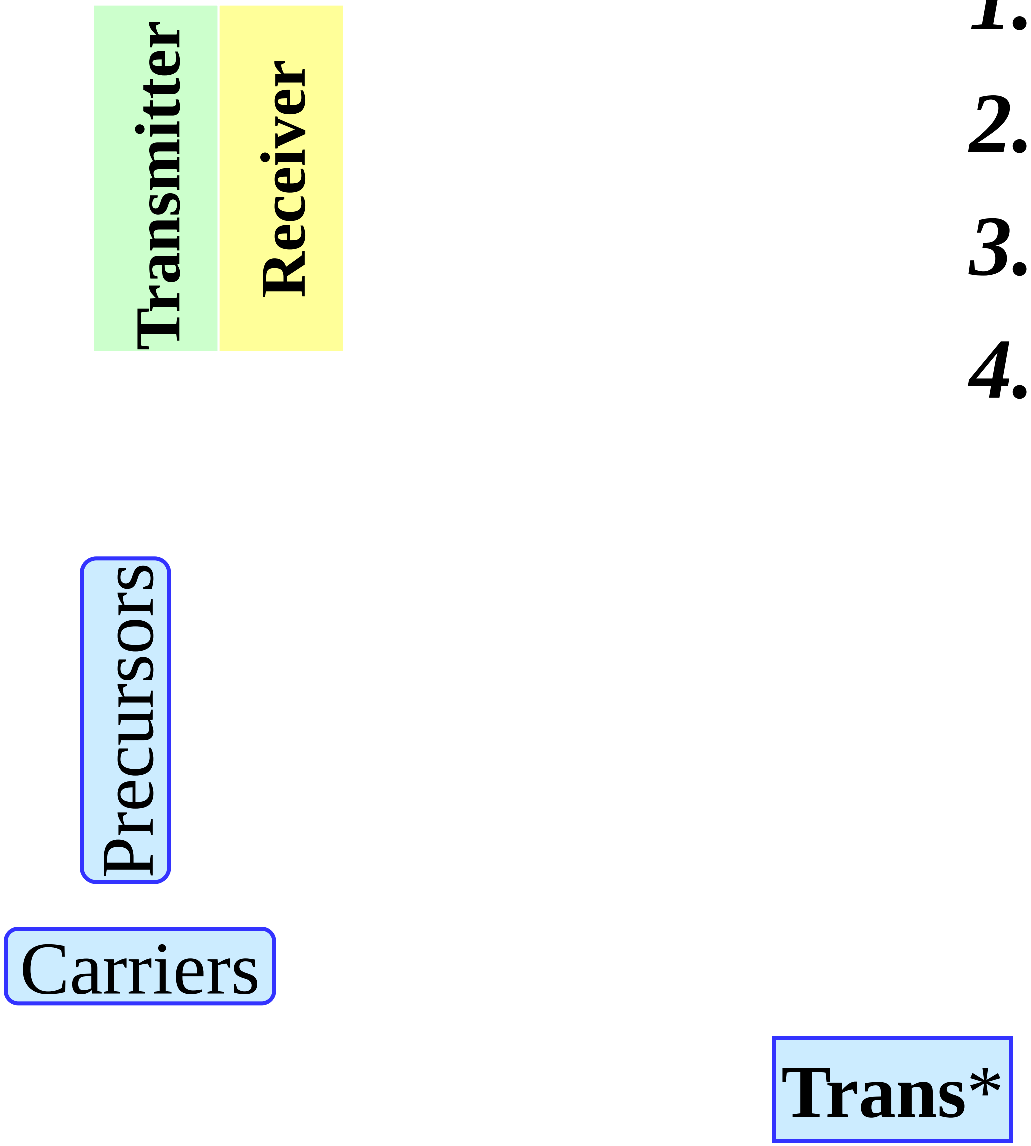


1. *Carriers*
2. *Precursors*
3. *Trans**
4. *2CST*

Bacterial bowties



1. ***Carriers***
2. ***Precursors***
3. ***Trans****
4. ***2CST***



Transmitter

Receiver

Constraints

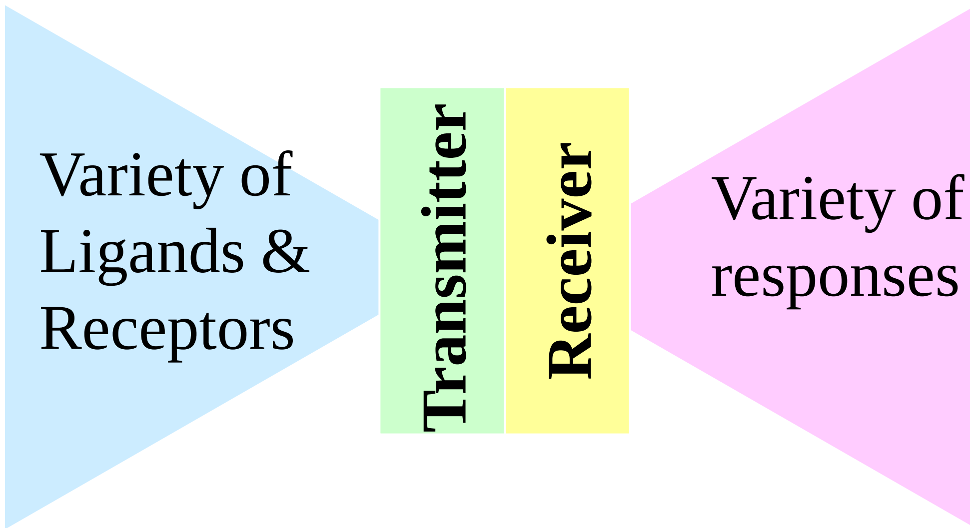
Precursors

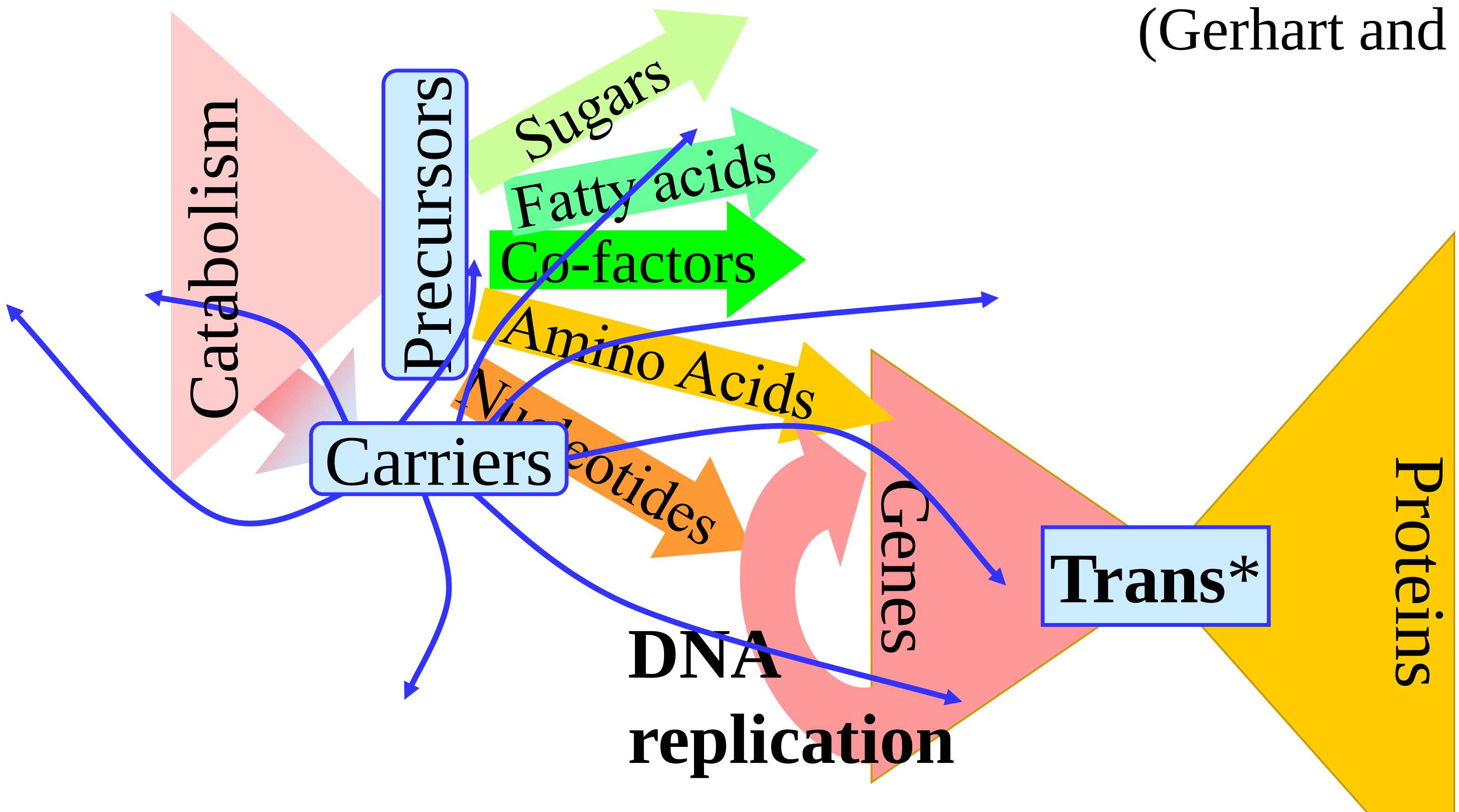
Carriers

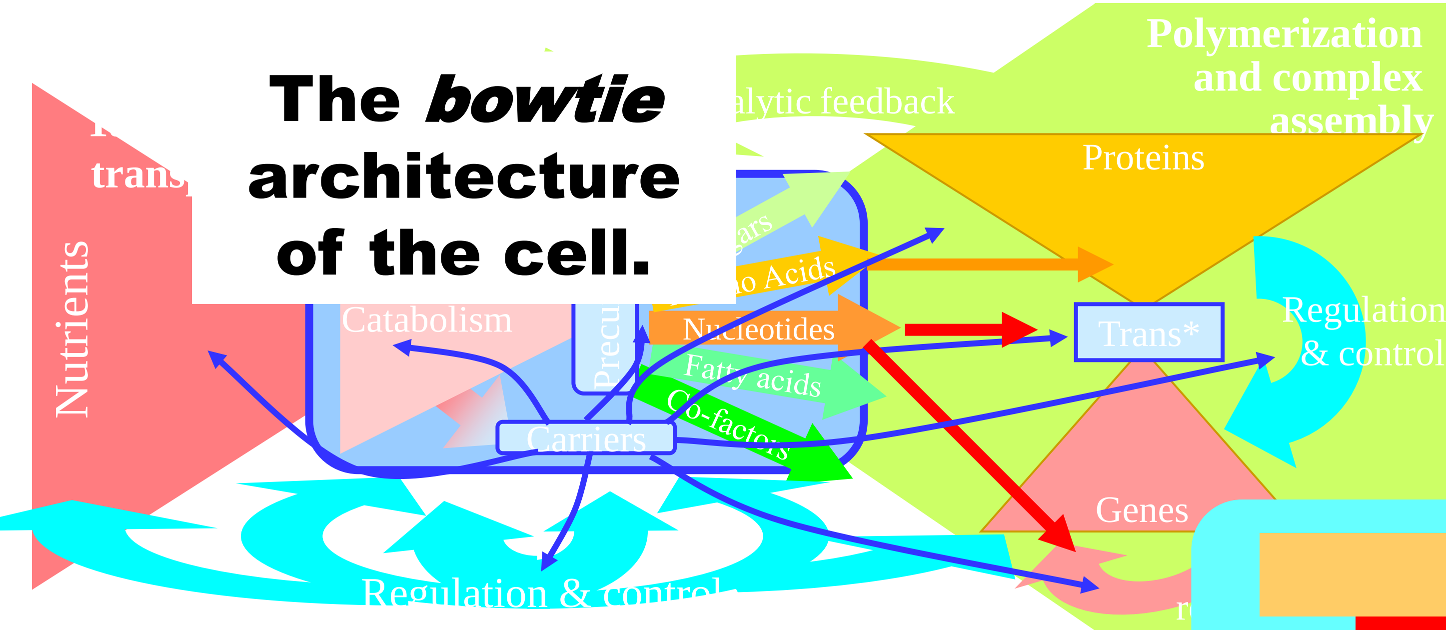
Trans*

Constraints That Deconstrain

(Gerhart and Kirschner)



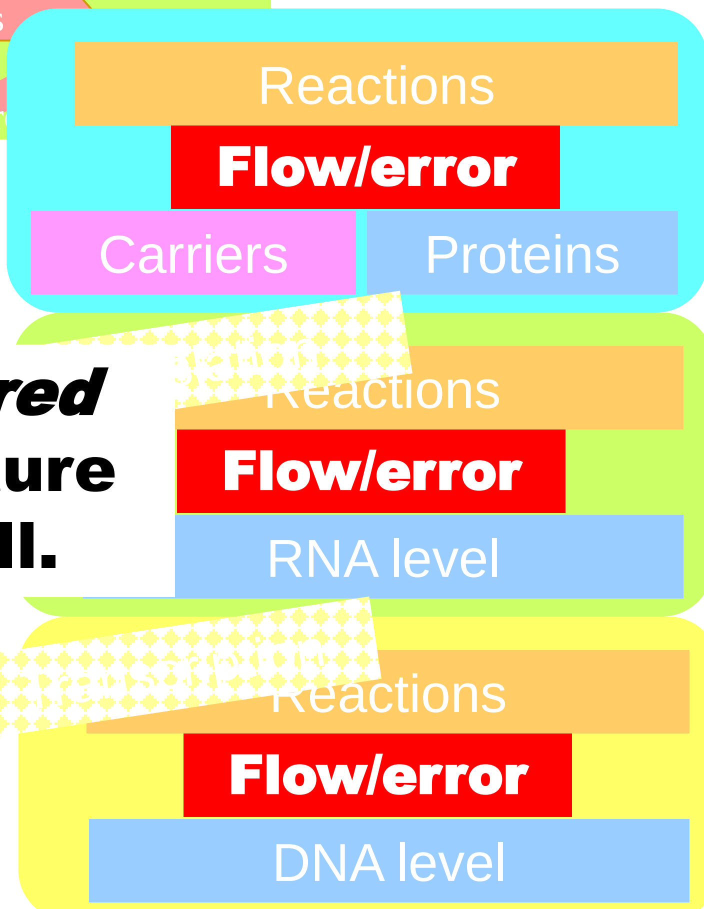


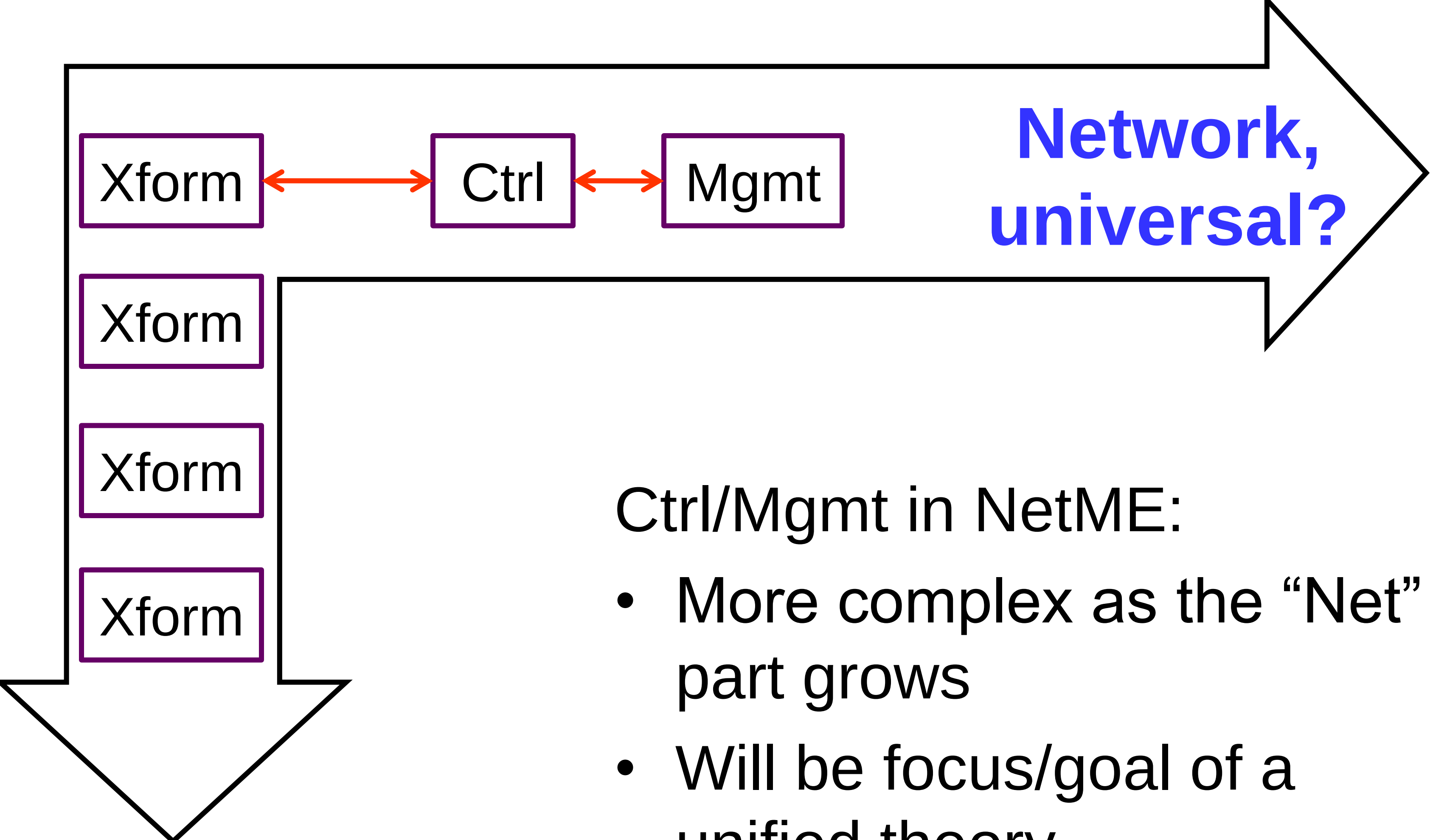


The *bowtie* architecture of the cell.

Need a more coherent cartoon to visualize how these fit together.

The *layered* architecture of the cell.

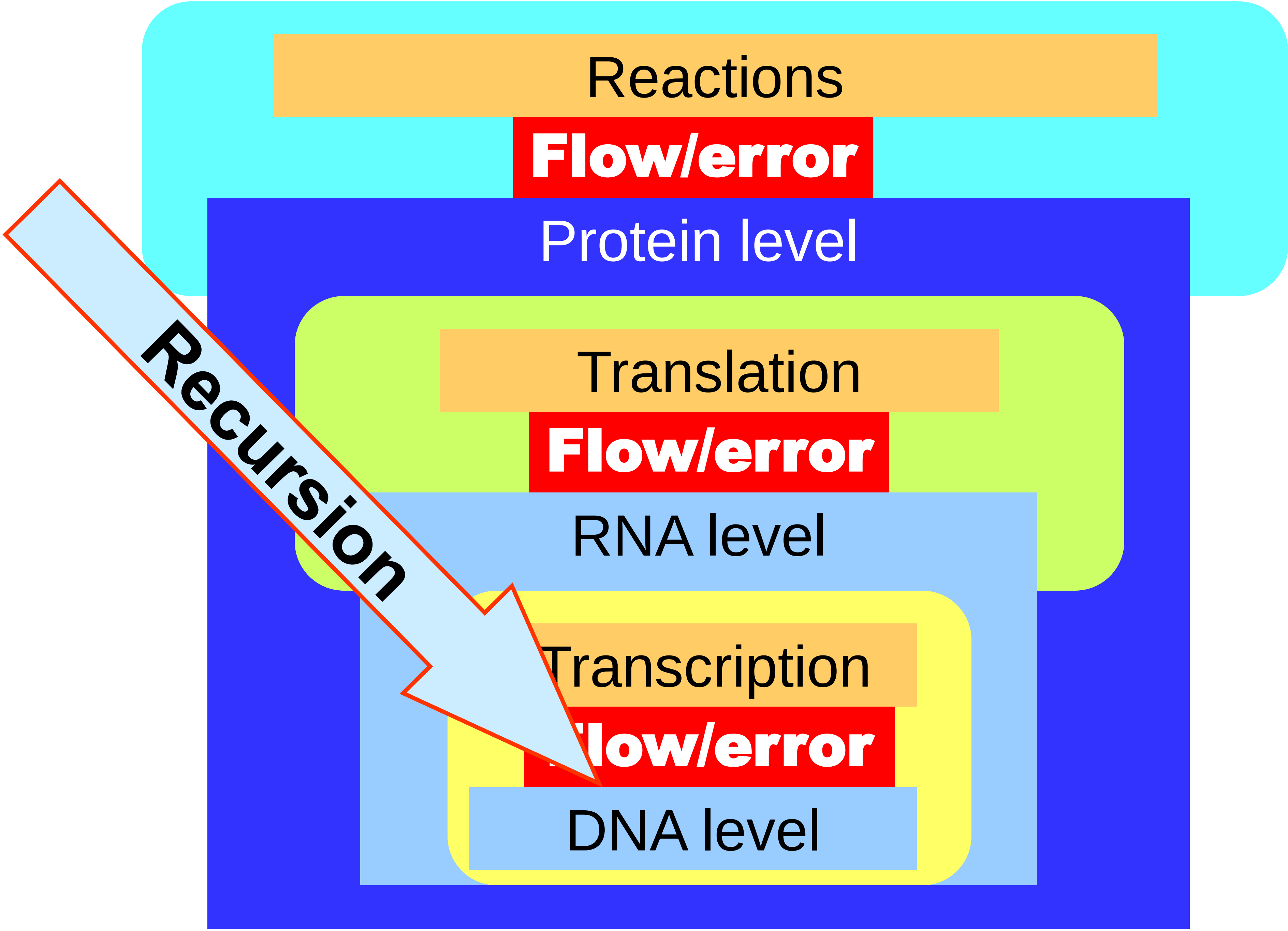




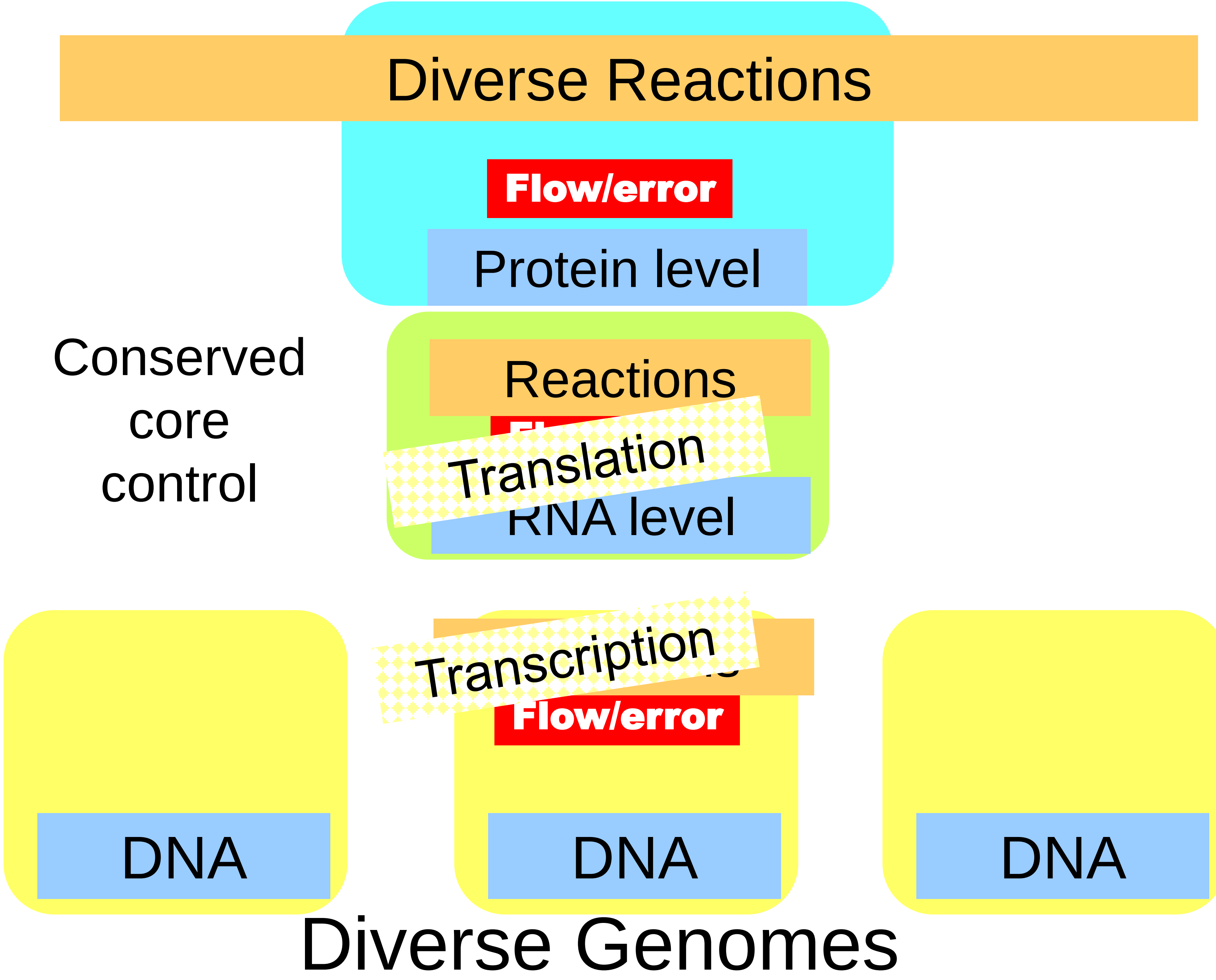
Domain specific, local

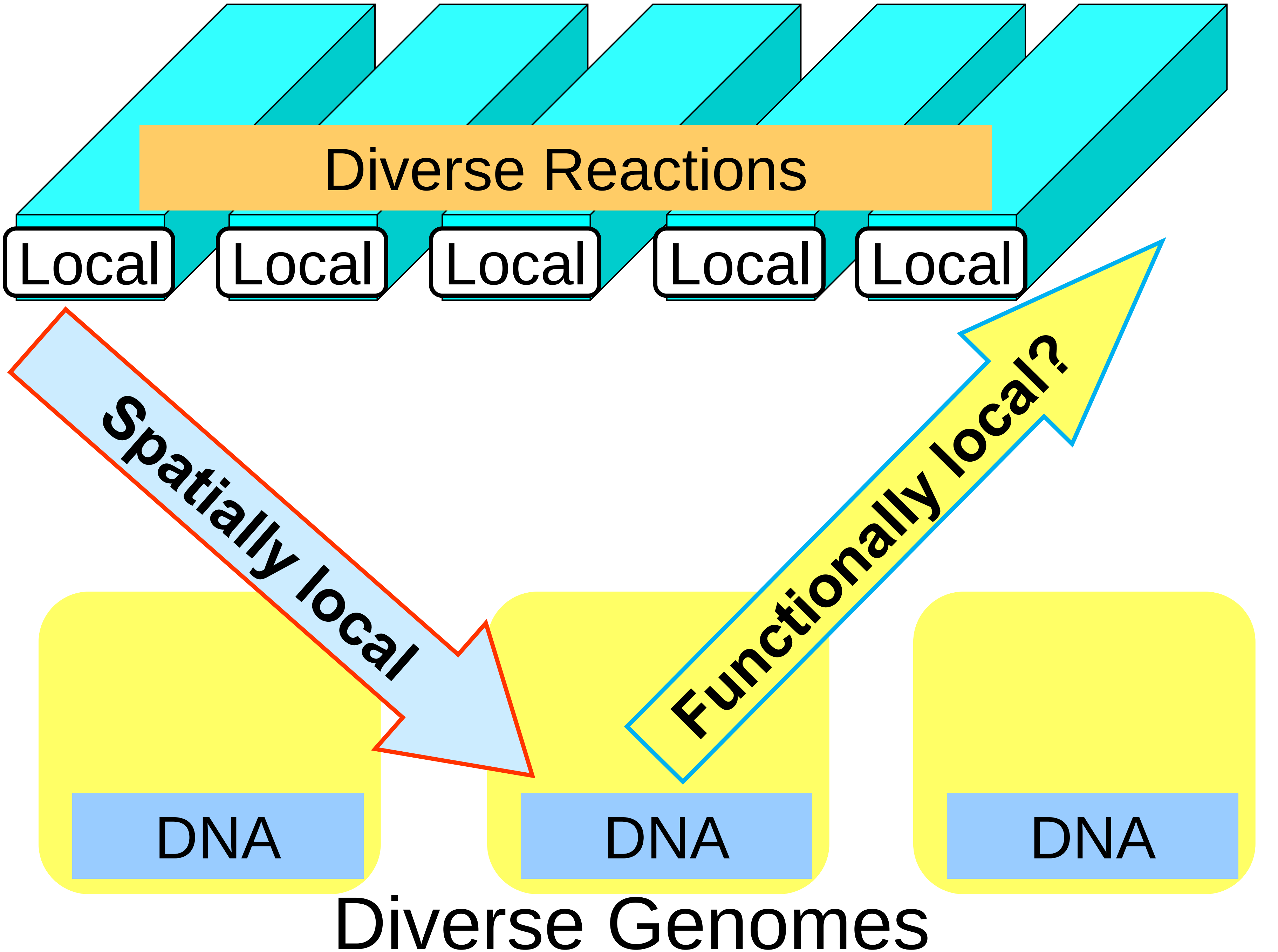
Ctrl/Mgmt in NetME:

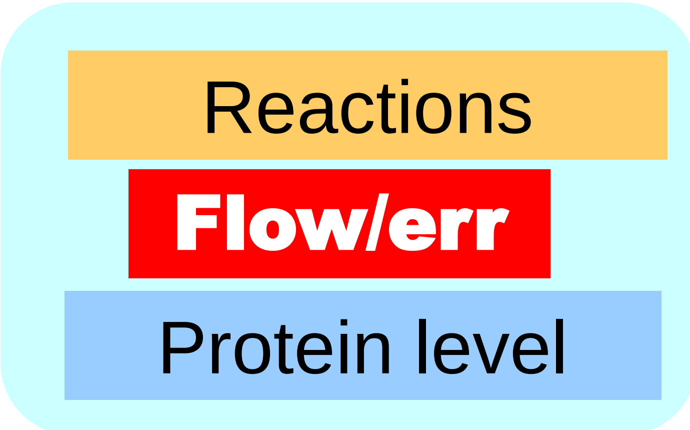
- More complex as the “Net” part grows
- Will be focus/goal of a unified theory
- From physics to information to computation to control

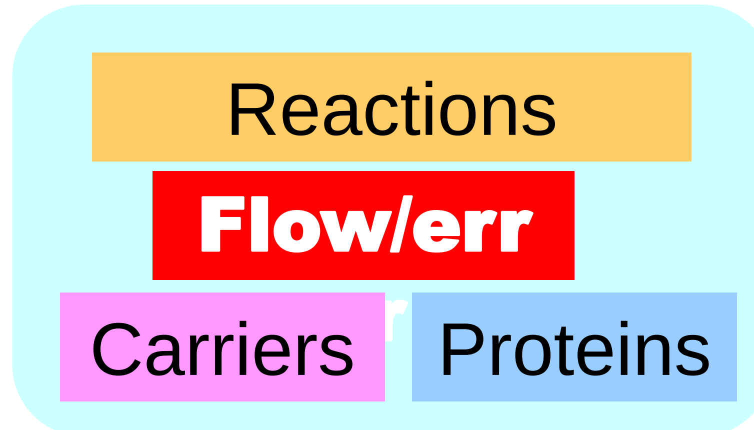


Reactions
Flow/error
Protein level
Translation
Flow/error
RNA level
Transcription
Flow/error
DNA level
Recursion

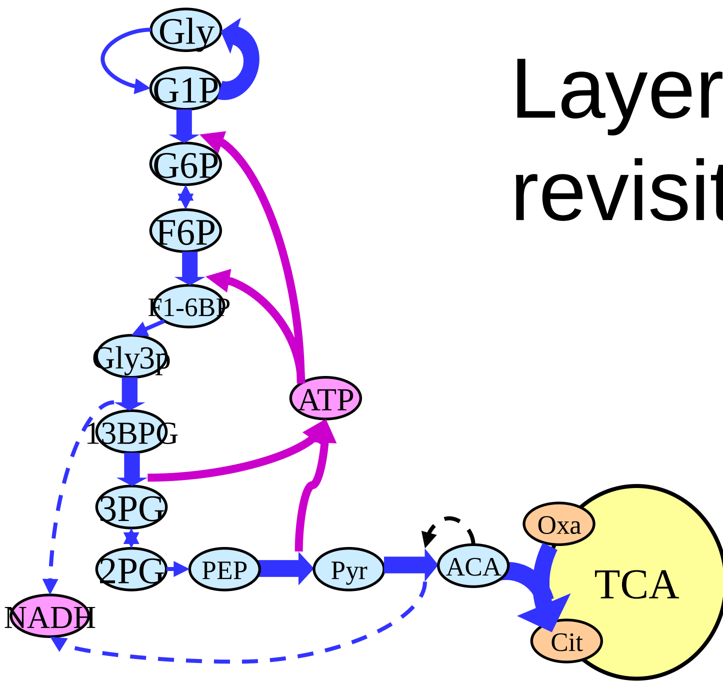

Diverse Reactions
Flow/error
Protein level
Conserved
core
control
Reactions
Translation
RNA level
Transcription
Flow/error
DNA
DNA
DNA
Diverse Genomes


Diverse Reactions
Local
Local
Local
Local
Local
Spatially local
Functionally local?
DNA
DNA
DNA
Diverse Genomes





Layering revisited



More complete picture

Biology versus the Internet

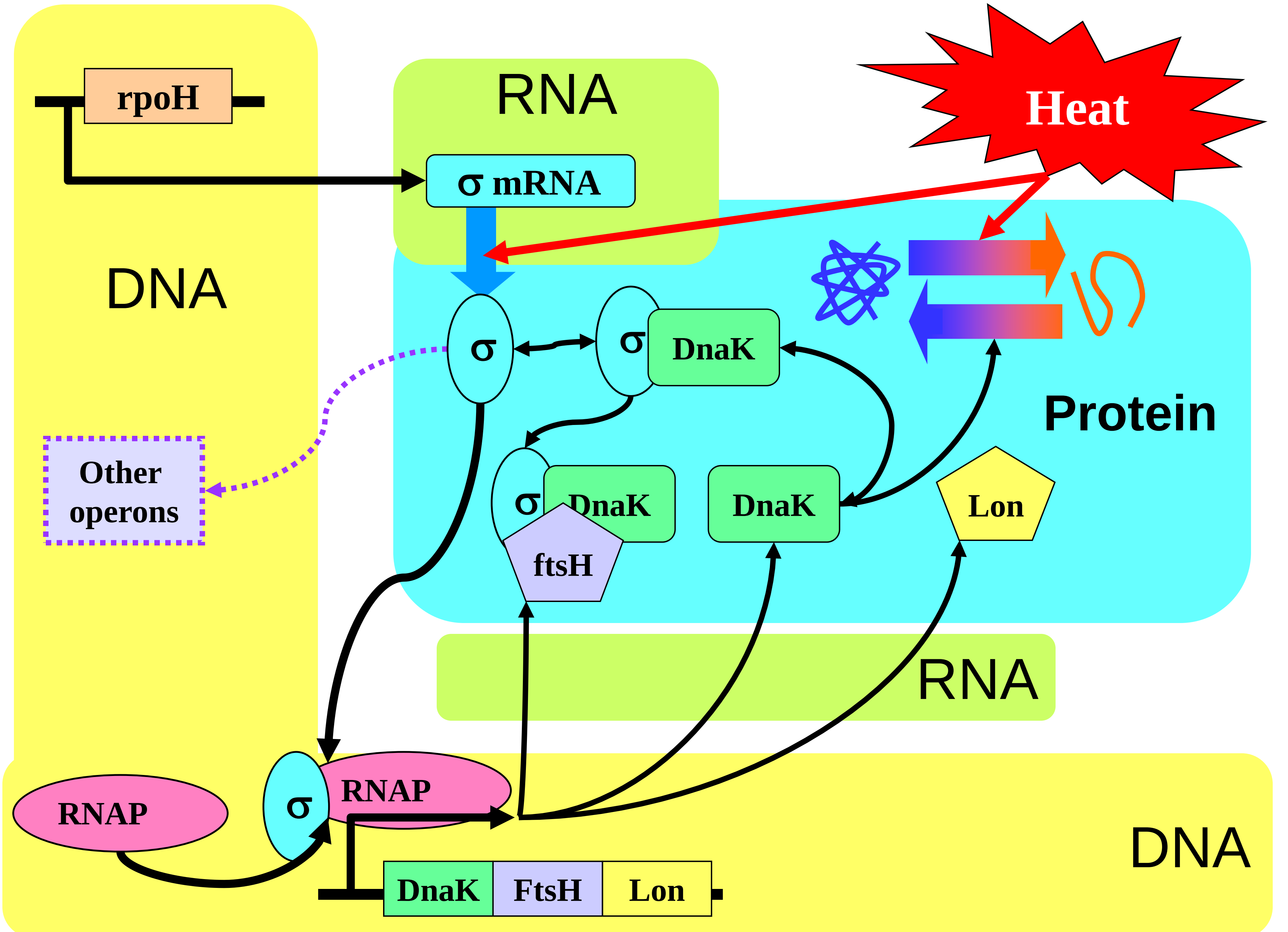
Similarities

- Evolvable architecture
- Robust yet fragile
- **Layering, modularity**
- Hourglass with bowties
- Dynamics
- Feedback
- Distributed/decentralized

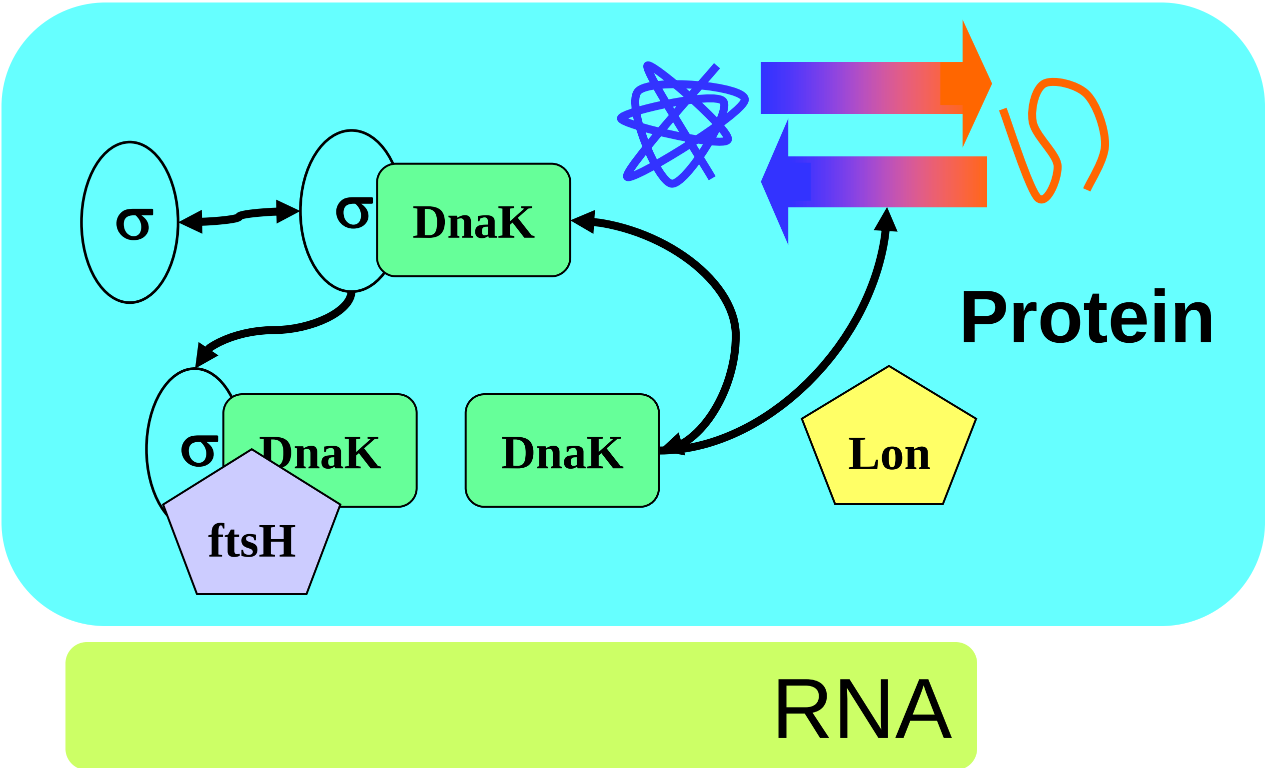
- ***Not*** scale-free, edge-of-chaos, self-organized criticality, etc

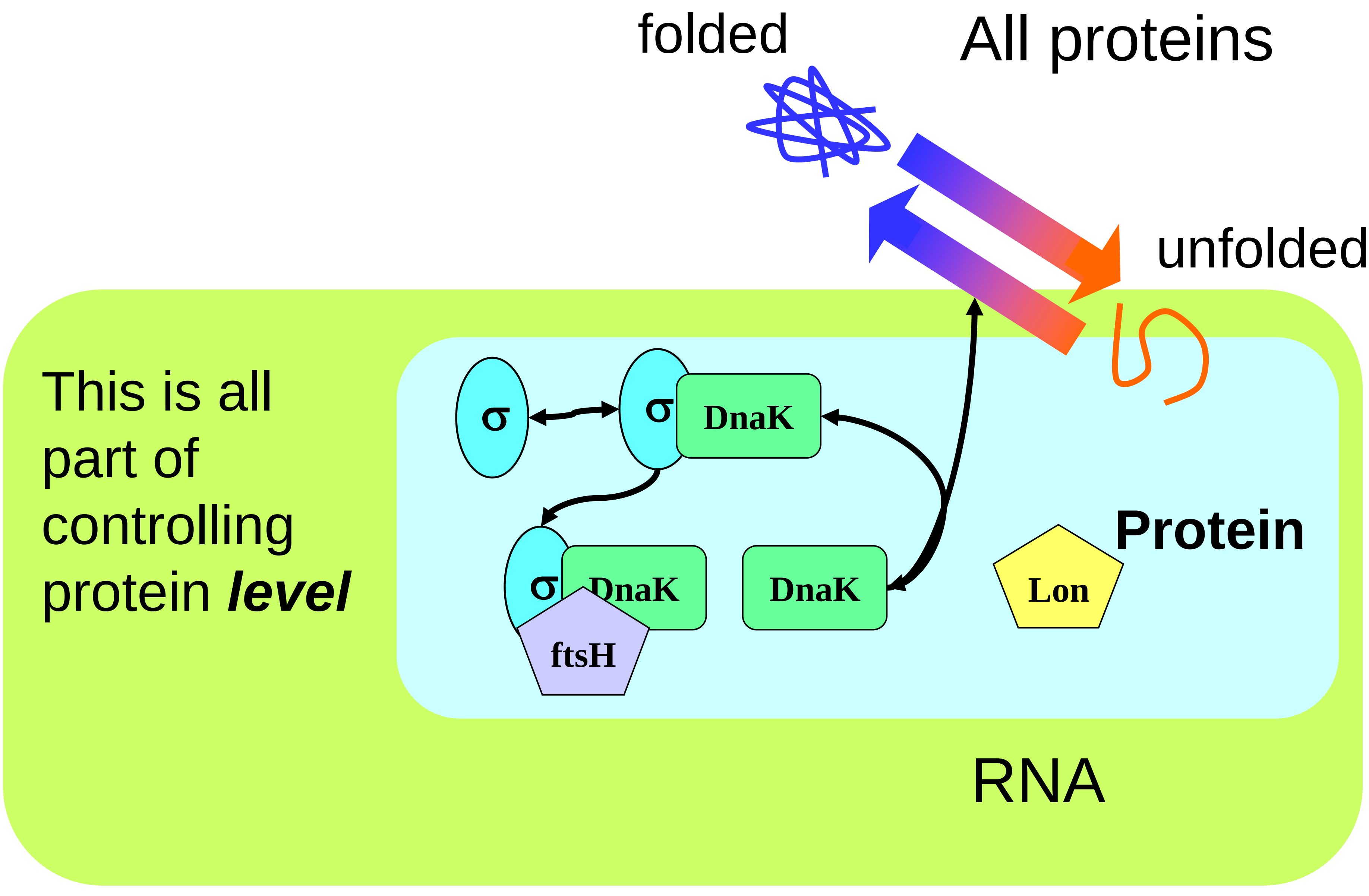
Differences

- Metabolism
- Materials and energy
- **Autocatalytic feedback**
- Feedback complexity
- Development and regeneration
- >3B years of evolution

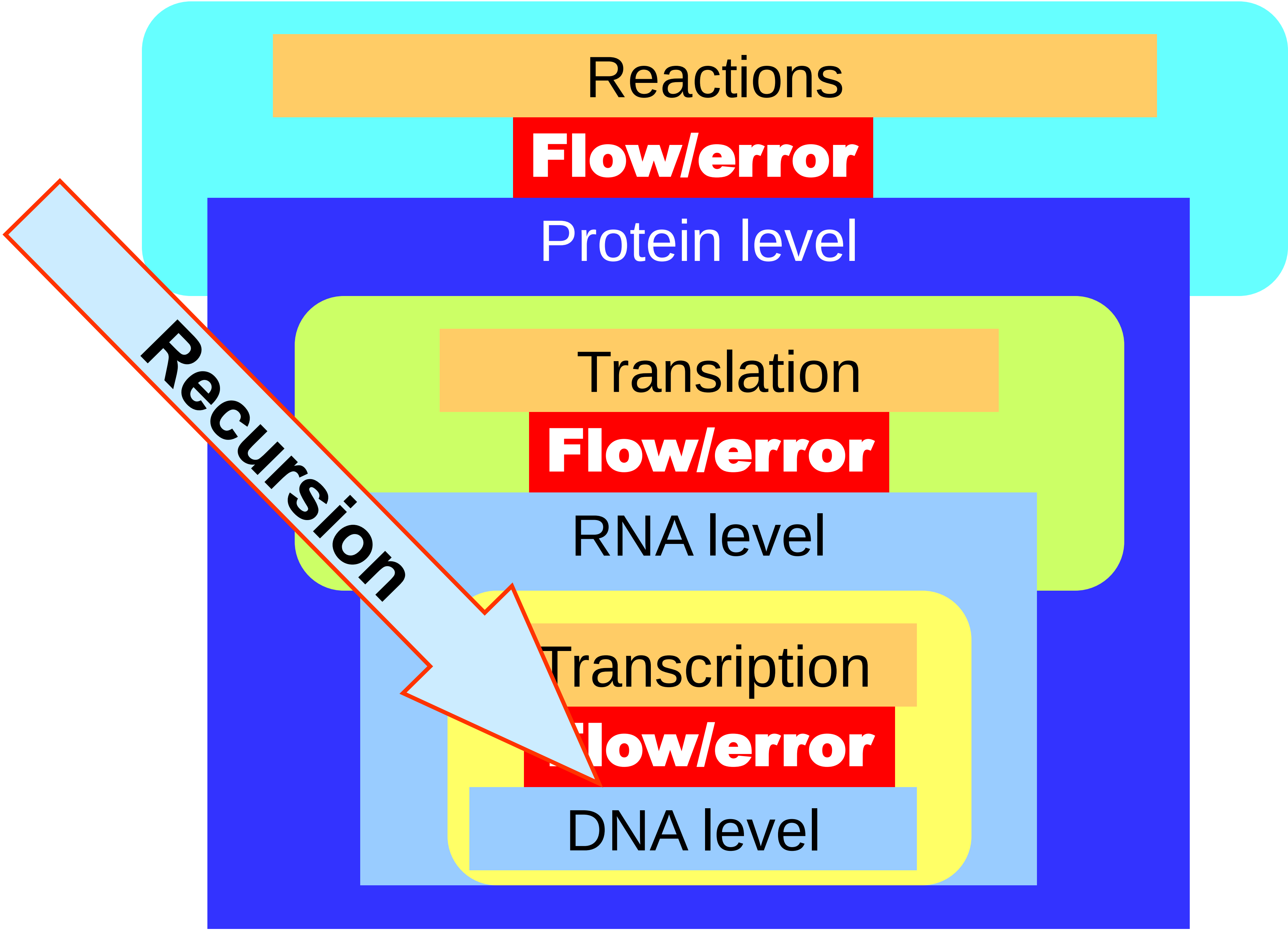


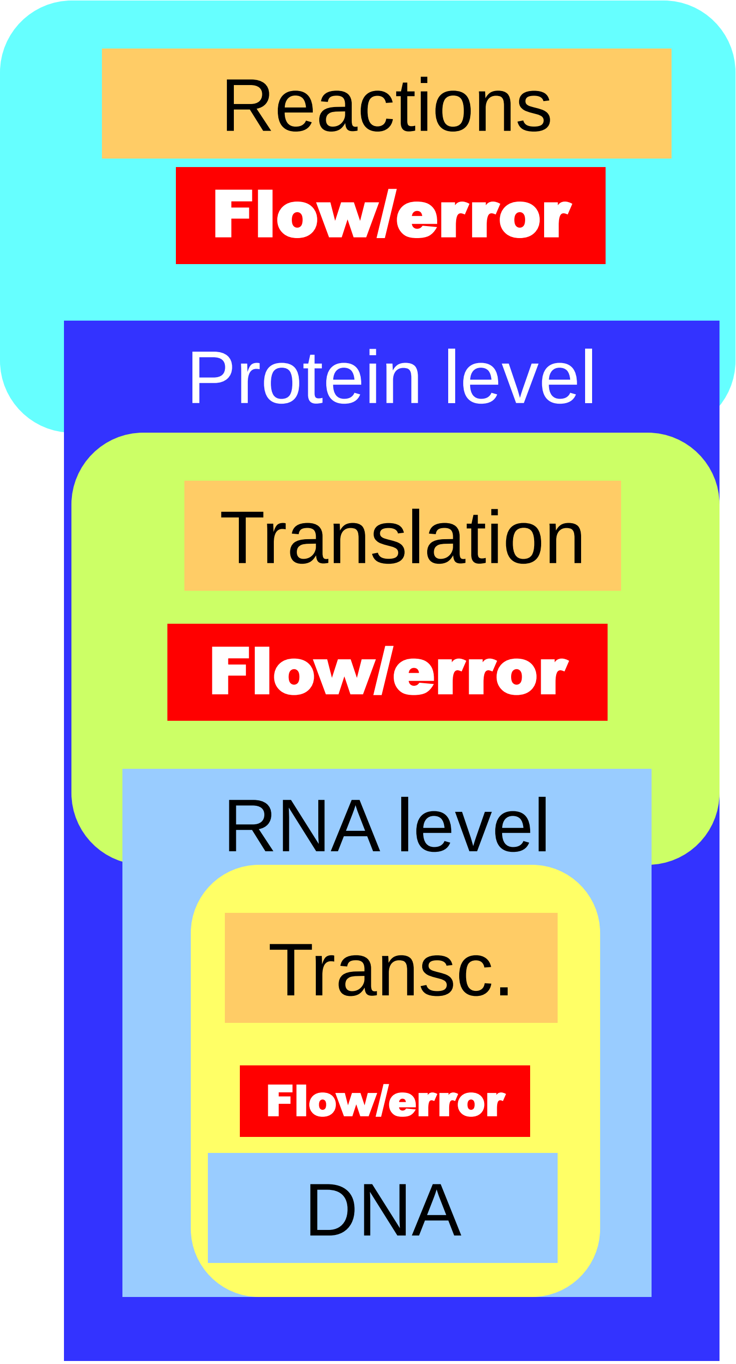
rpoH
RNA
σ mRNA
Heat
DNA
σ
σ
DnaK
Protein
Other operons
σ
DnaK
ftsH
DnaK
Lon
RNA
RNAP
σ
RNAP
DNA
DnaK
FtsH
Lon

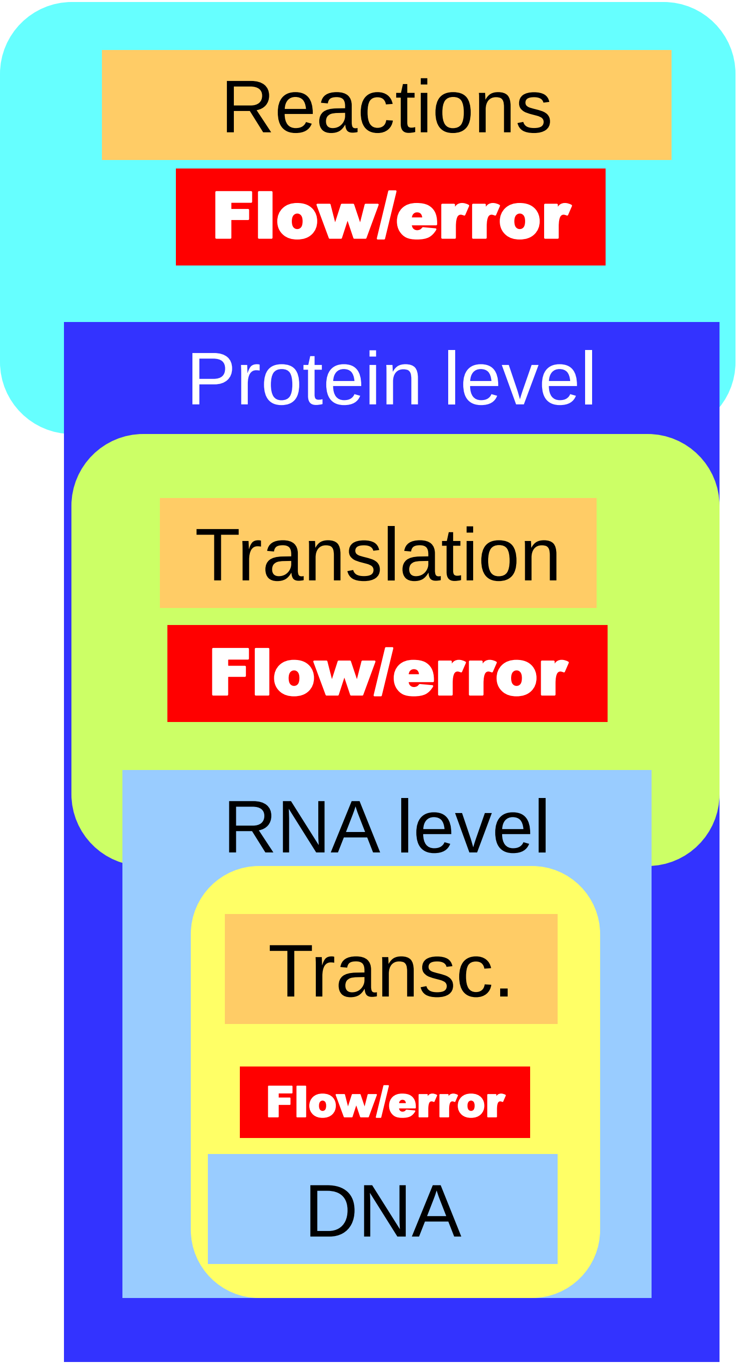

σ
σ
DnaK
Protein
σ
DnaK
DnaK
Lon
ftsH
RNA



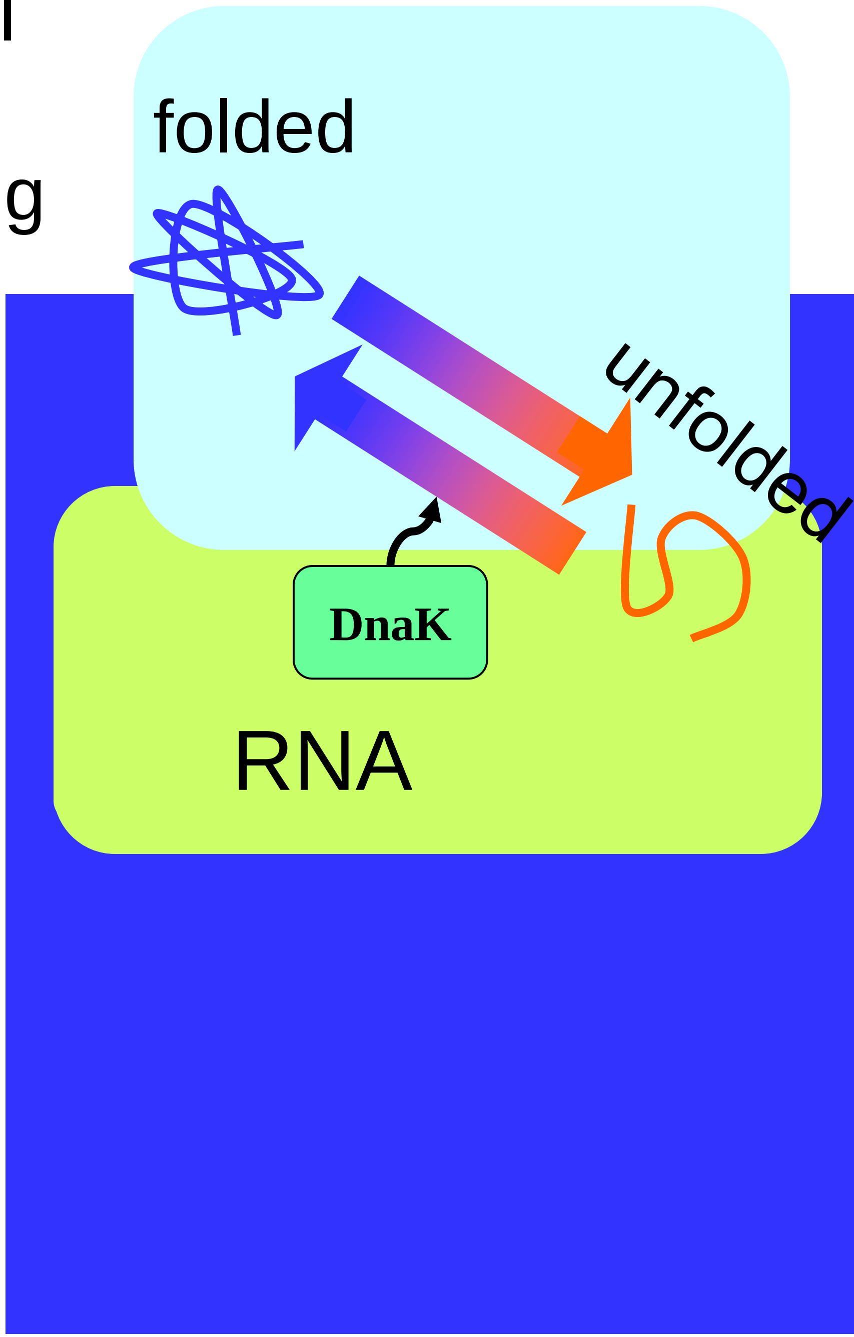
folded
All proteins
unfolded
This is all part of controlling protein ***level***
σ
σ
DnaK
σ
DnaK
ftsH
DnaK
Lon
Protein
RNA


Reactions
Flow/error
Protein level
Translation
Flow/error
RNA level
Transcription
Flow/error
DNA level
Recursion

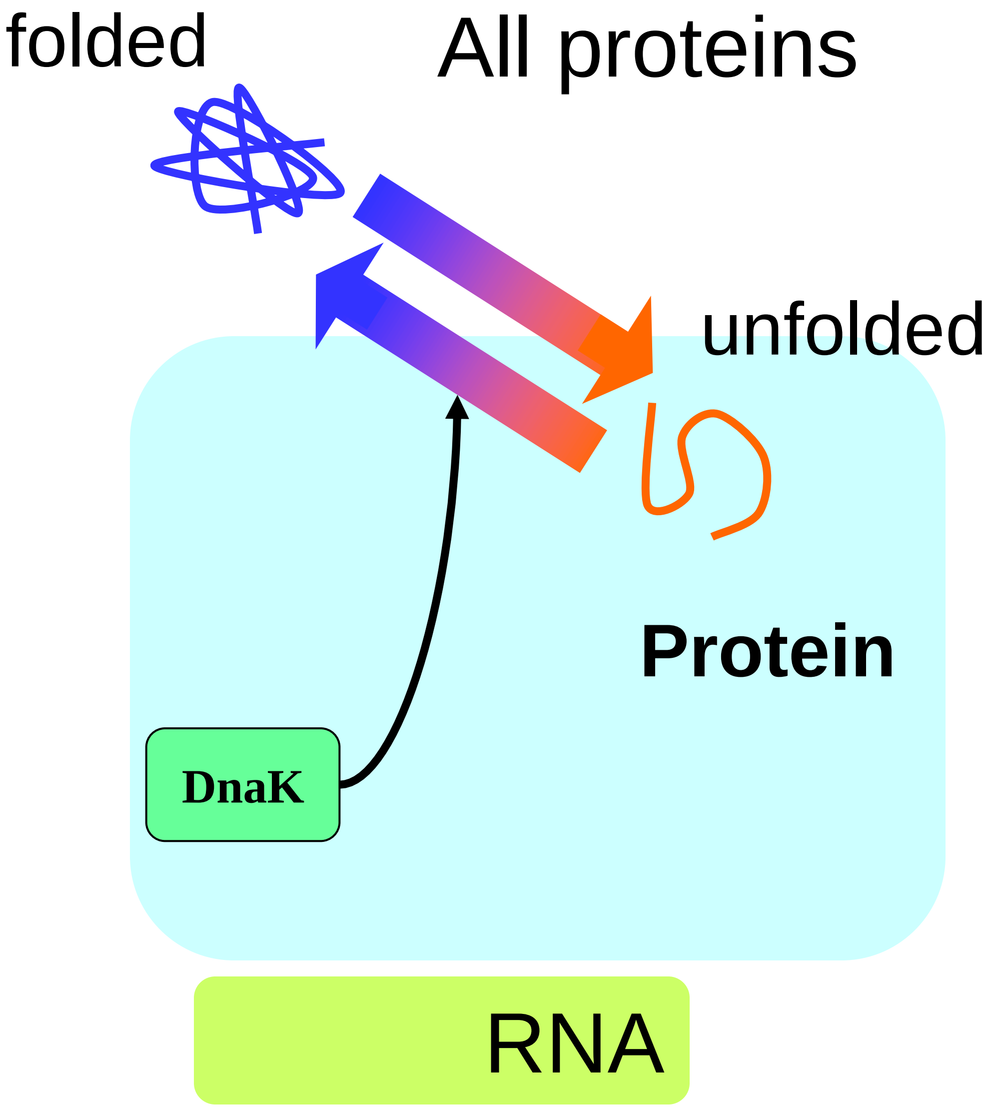

Reactions
Flow/error
Protein level
Translation
Flow/error
RNA level
Transc.
Flow/error
DNA

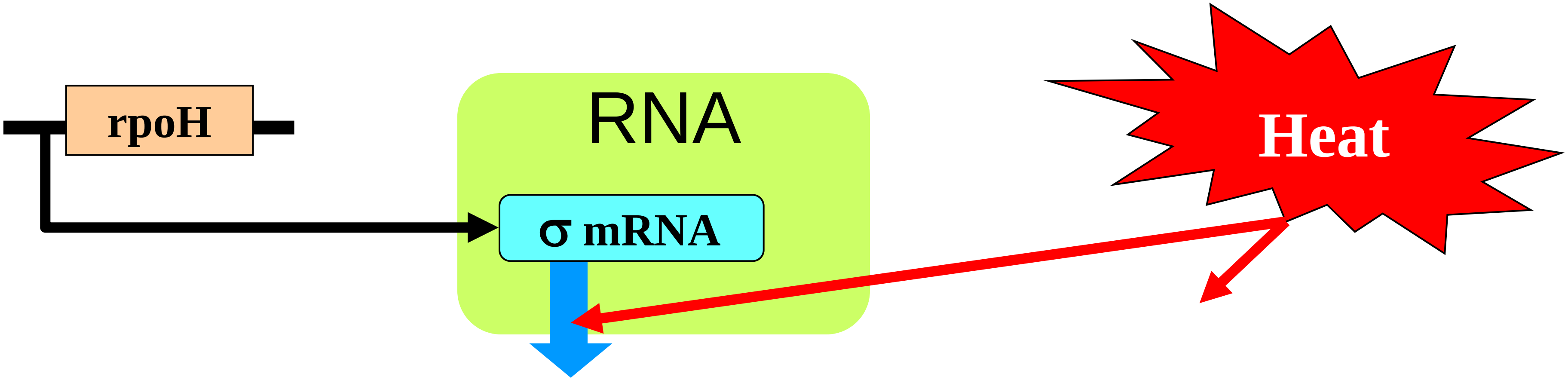


This is all part of controlling protein ***level***



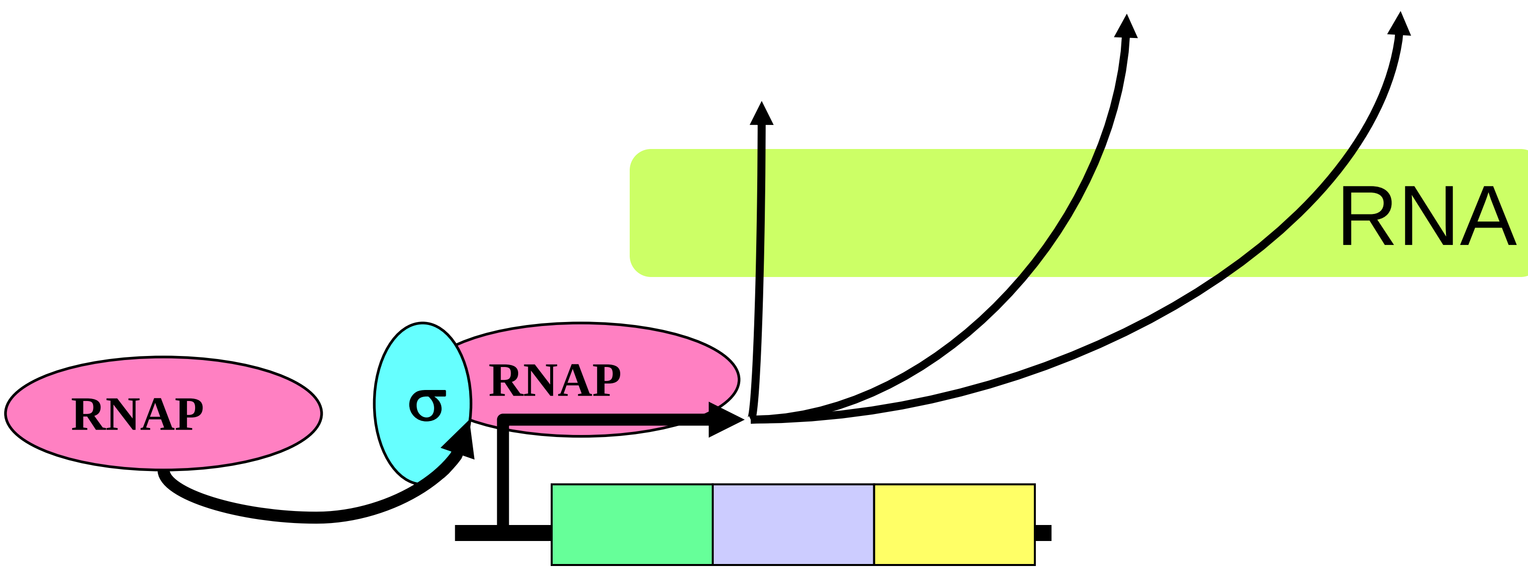
This is all
part of
controlling
protein level

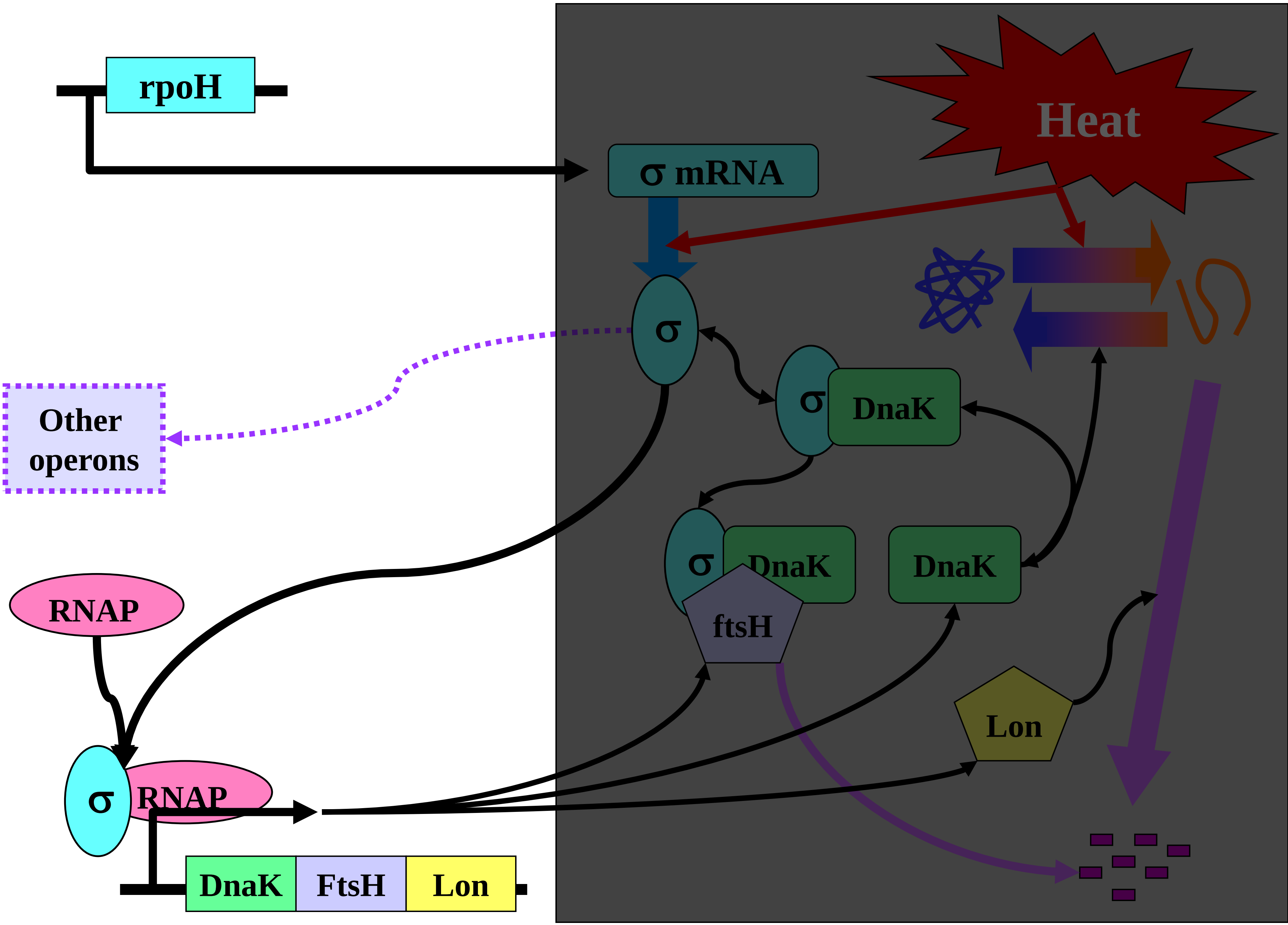


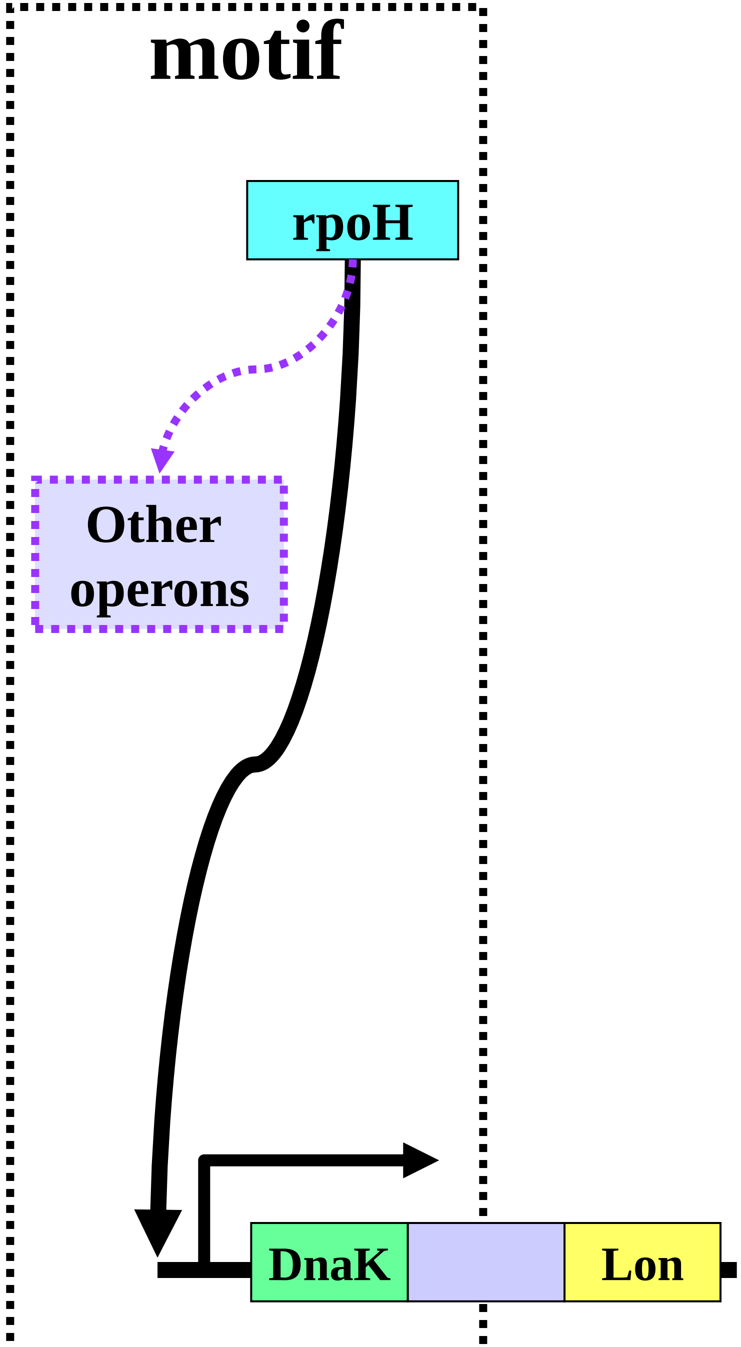


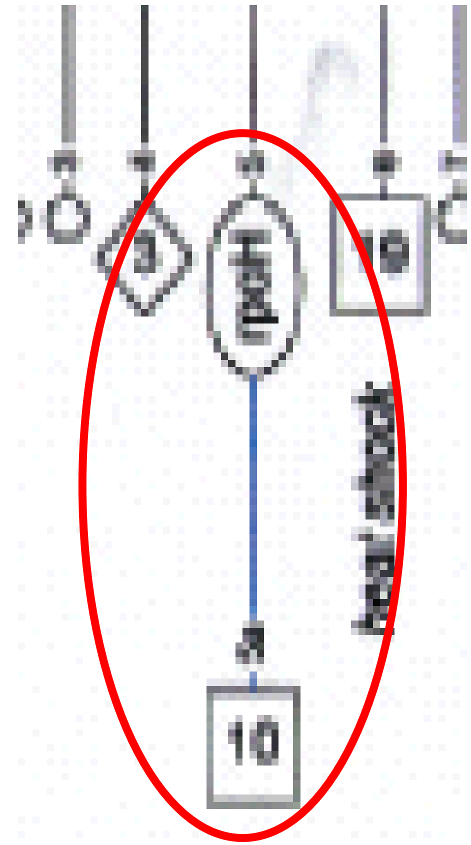
mRNA activity is actively controlled.

Translation was not shown.

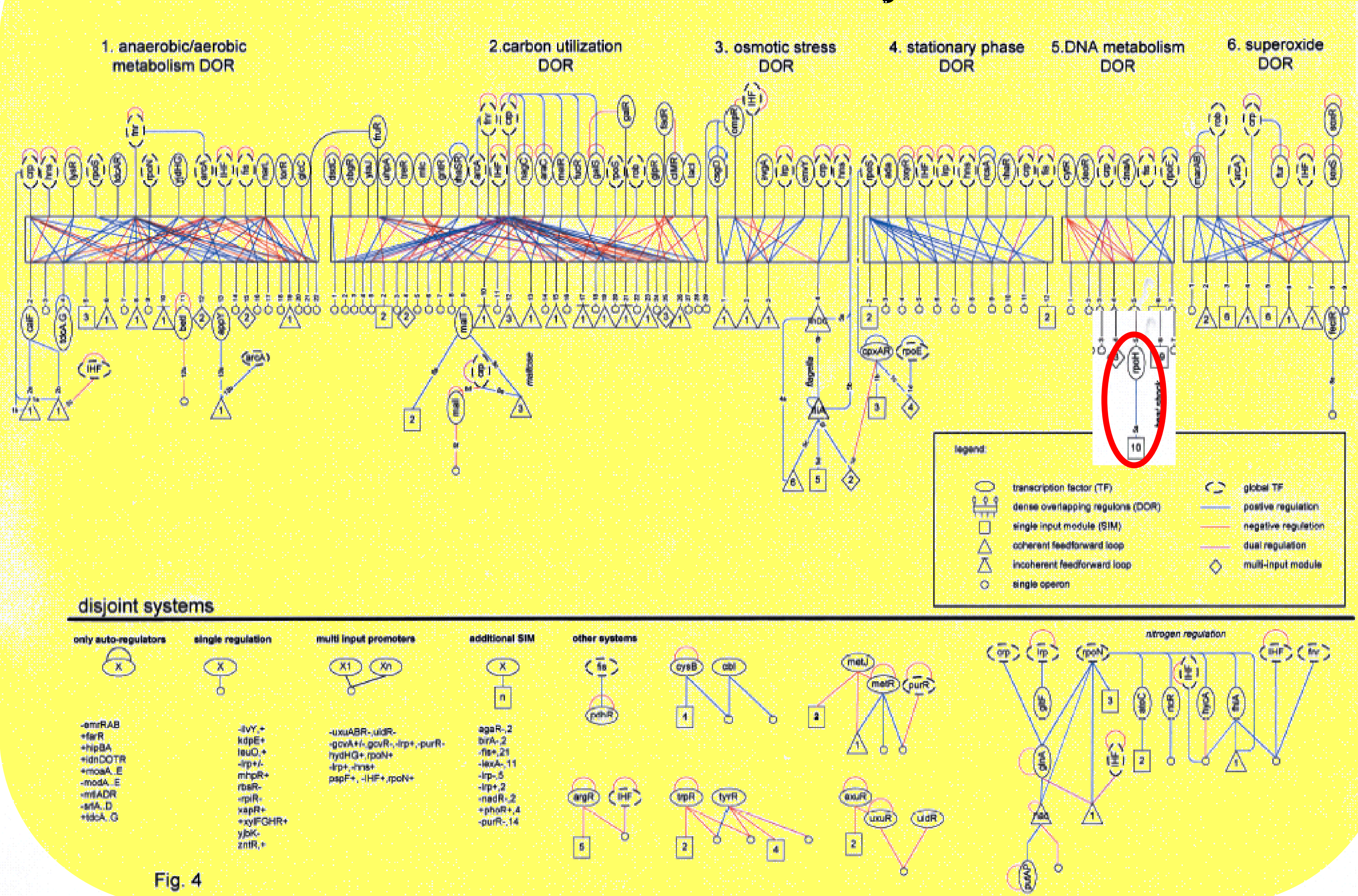


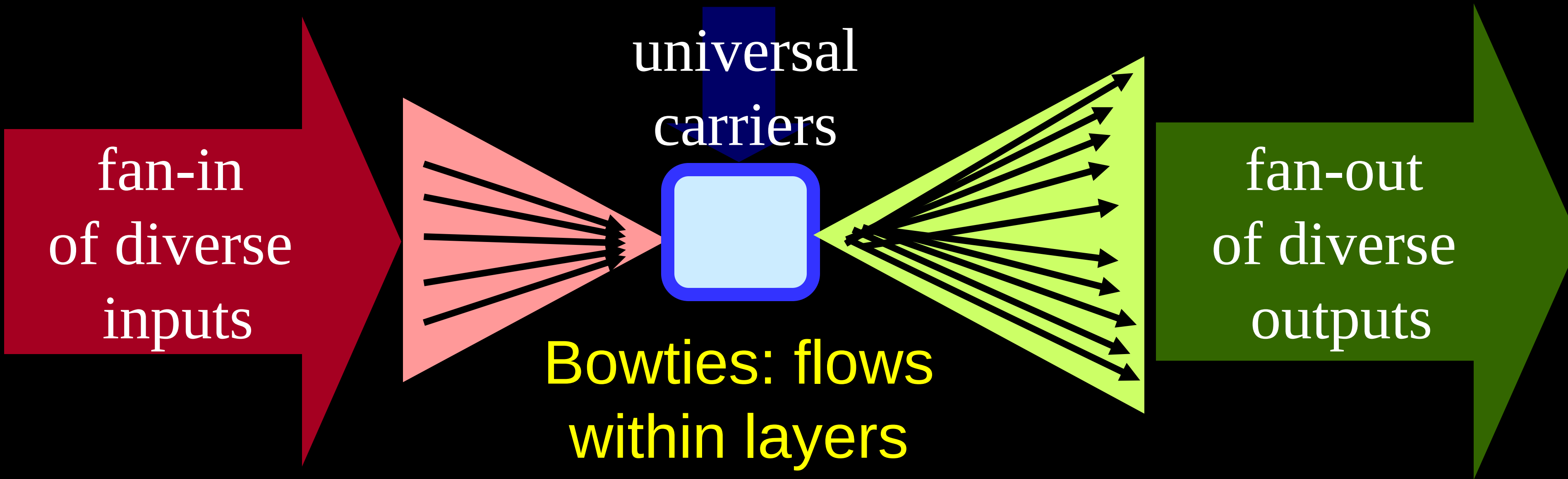

rpoH
σ mRNA
Heat
σ
Other operons
σ
DnaK
σ
DnaK
DnaK
ftsH
Lon
RNAP
σ
RNAP
DnaK
FtsH
Lon

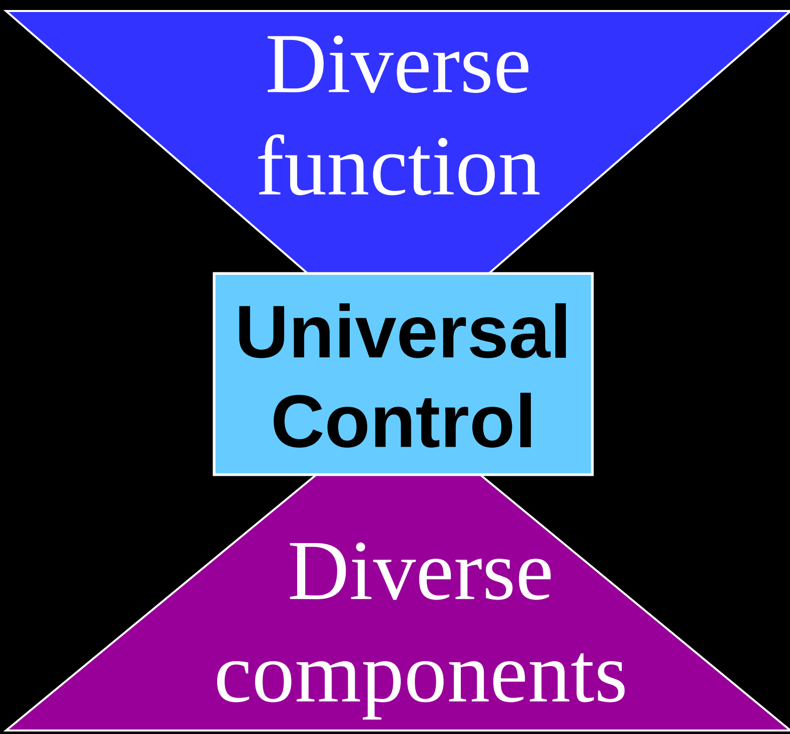

motif
rpoH
Other operons
DnaK
Lon


10

All at the DNA layer



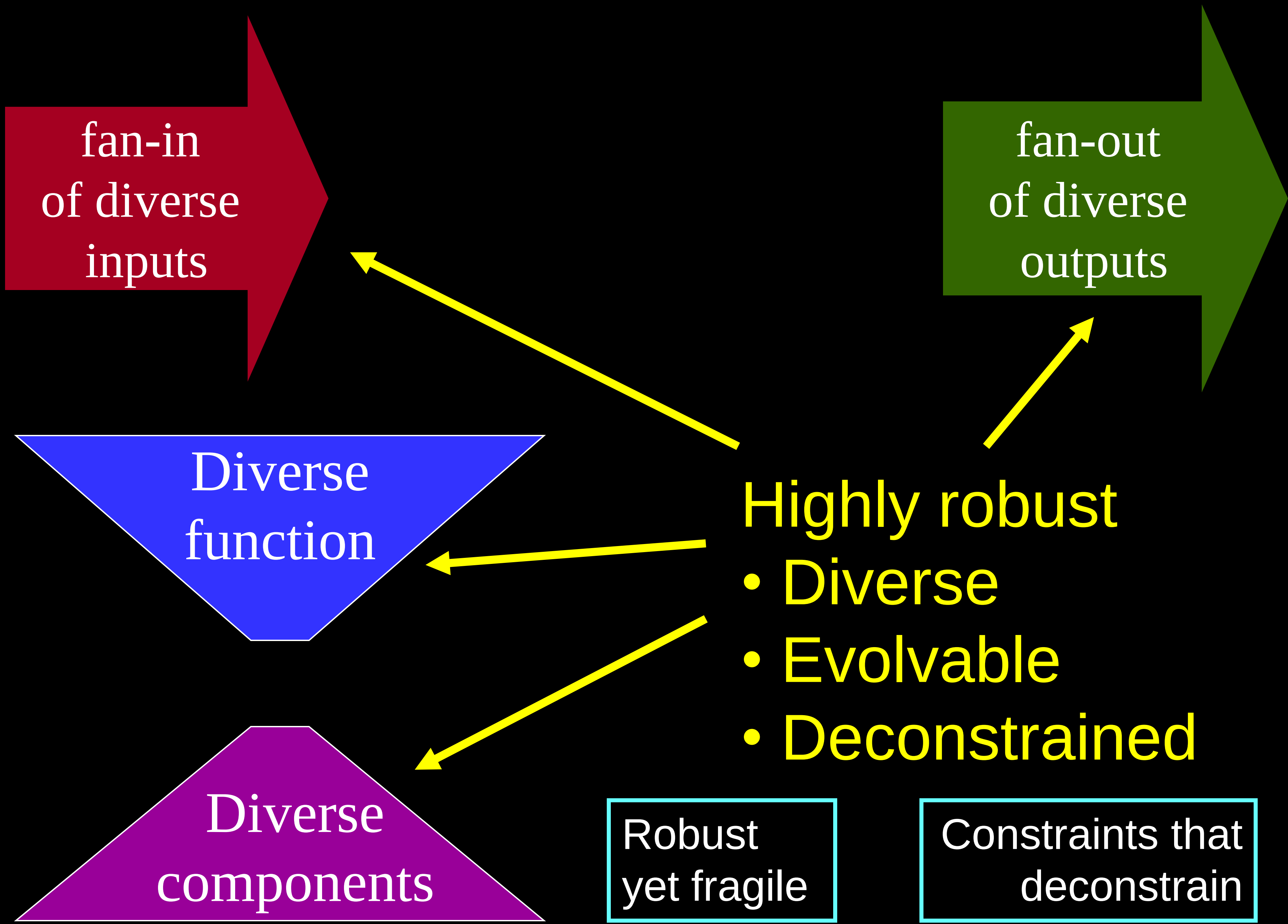


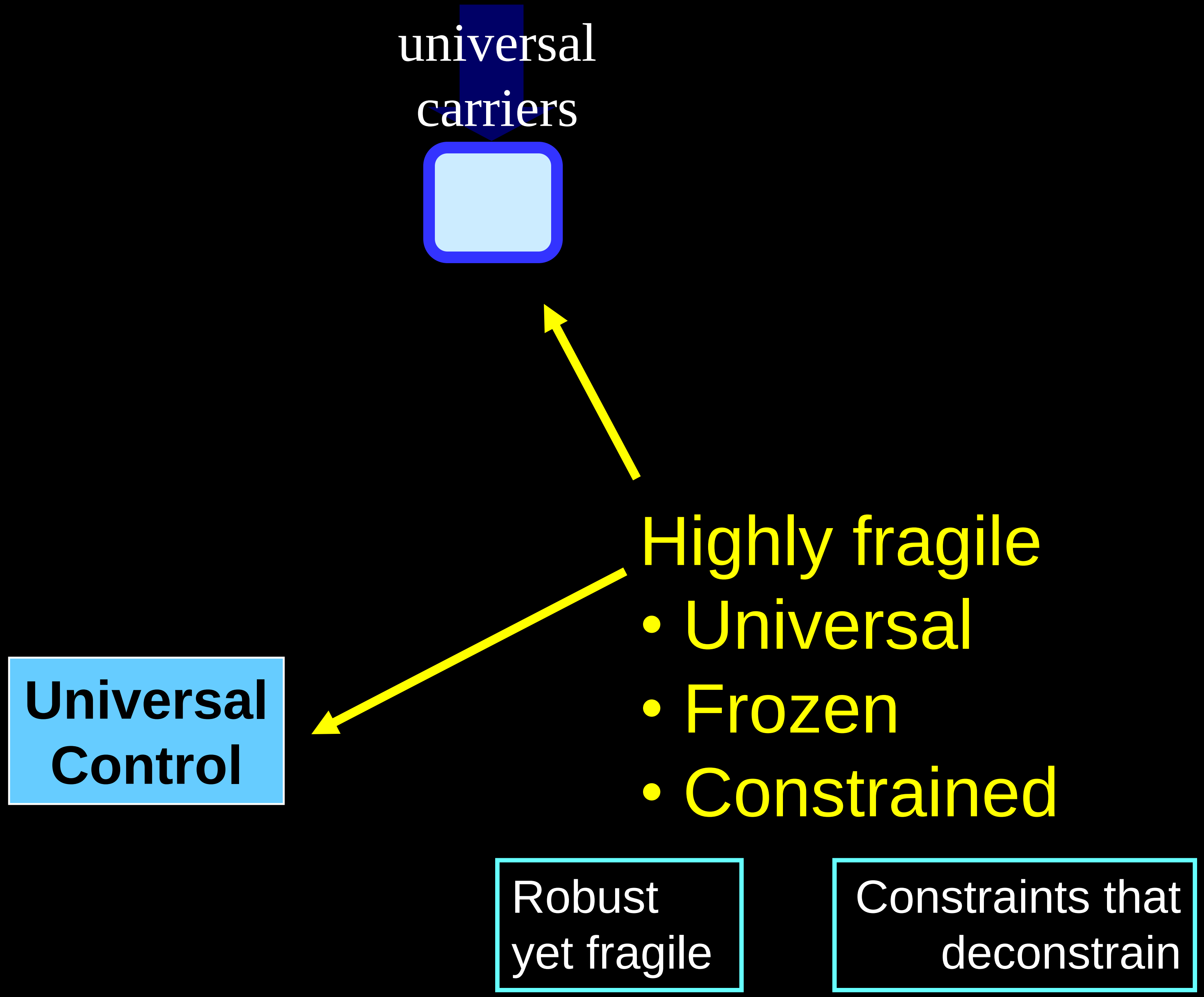


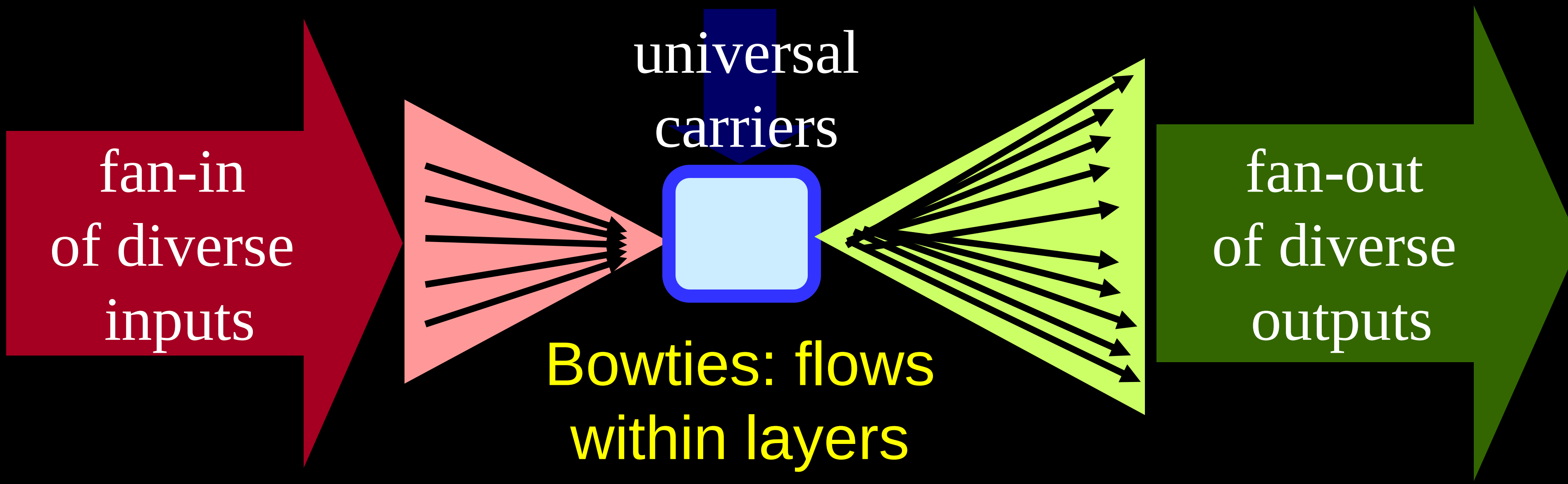
Essential ideas

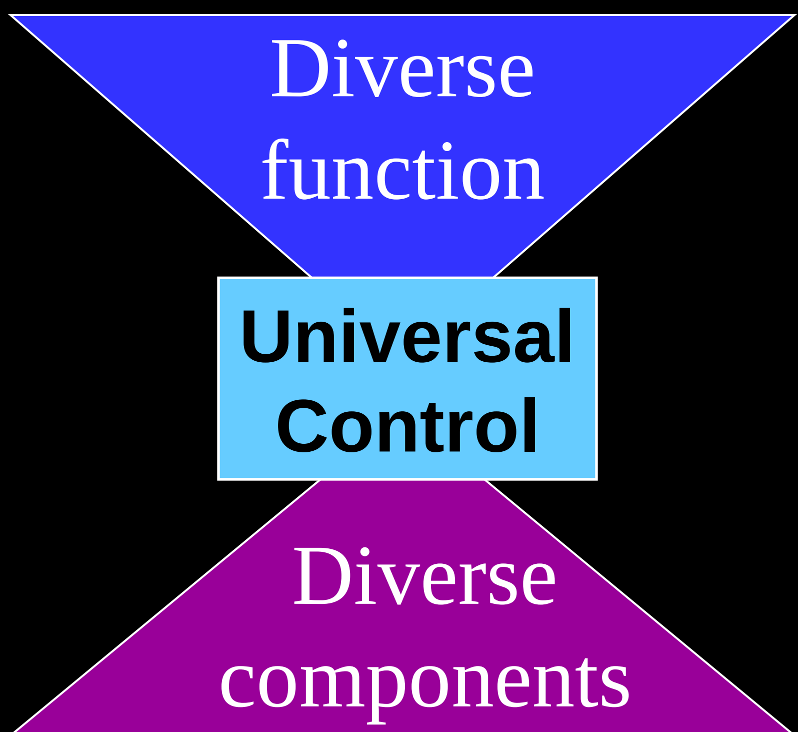
Robust yet fragile

Constraints that deconstrain


fan-in
of diverse
inputs
fan-out
of diverse
outputs
Diverse
function
Highly robust
• Diverse
• Evolvable
• Deconstrained
Diverse
components
Robust
yet fragile
Constraints that
deconstrain


universal
carriers
Highly fragile
• Universal
• Frozen
• Constrained
Universal Control
Robust yet fragile
Constraints that deconstrain





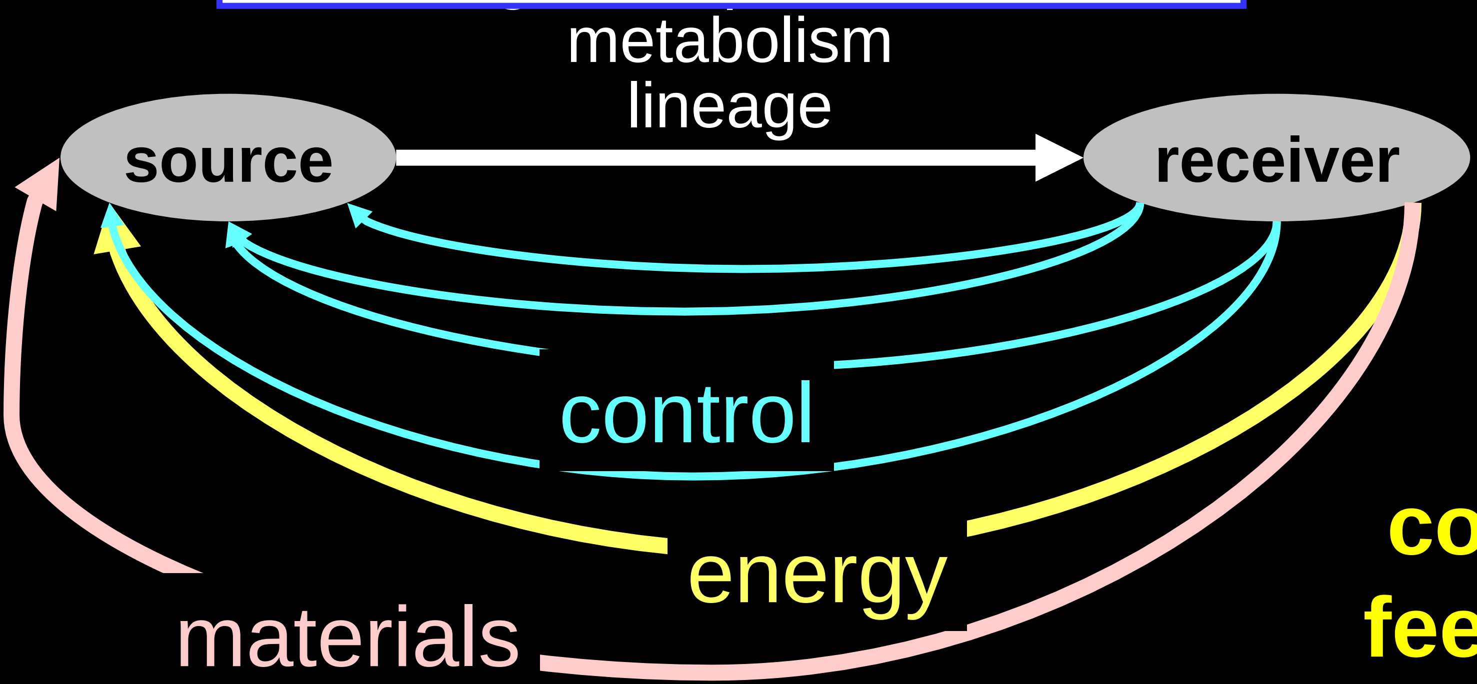
Essential ideas

Robust yet fragile

Constraints that deconstrain

What theory is relevant to these more complex feedback systems?

$$\frac{1}{\pi}\int_0^\infty \ln\left|S(j\omega)\right|\frac{z}{z^2+\omega^2}d\omega \geq \ln\left|\frac{z+p}{z-p}\right|$$



More complex feedback

New fragilities

- Theft, counterfeiting, fraud, and “creative accounting” are now possible
- Need complex legal infrastructure to protect
- The beginning of a growing complexity-fragility spiral